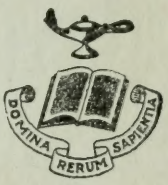


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# TRANSACTIONS

OF THE

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1921

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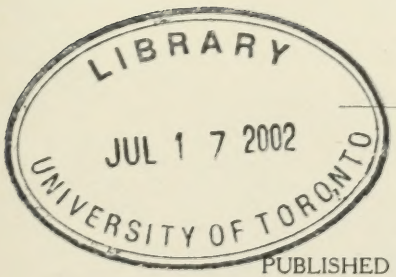

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# 20th ANNUAL MEETING

## Marlboro-Blenheim

## Atlantic City, June 6th and 7th, 1919

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| *Carl Beck | New York, N. Y. | 1905-6 |
| *Robert Reyburn | Washington, D. C. | 1906-7 |
| *John V. Shoemaker | Philadelphia, Pa. | 1907-8 |
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| W. Wayne Babcock | Philadelphia, Pa. | 1917-18 |
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| C. E. DeM. Sajous | Philadelphia, Pa. | 1919-20 |

*Deceased.

## DECEASED MEMBERS

Samuel Claggett Busey, M.D., LL.D., died Oct. 19, 1899.
William P. Manning, M.D., died Feb. 9, 1901.
John Thomas Winter, M.D., LL.D., died June 22, 1902.
George Edward Tyler, M.D., died July 7, 1902.
Robert Henderson Graham, M.D., died Aug. 24, 1903.
George Bingham Fowler, M.D., died March 6, 1907.
John S. McLain, M.D., died June 2, 1907.
Robert Reyburn, M.D., died March 25, 1909.
Justin Steer, M.D., died March 25, 1909.
Howard H. Barker, M.D., died May 8, 1910.
John Veitch Shoemaker, M.D., died October 11, 1910.
Carl Beck, M.D., died June 8, 1911.
Henry Alfred Robbins, M.D., died October 26, 1911.
John Herr Musser, M.D., died April 3, 1912.
Louis Nelson, A.M., M.D., died April 14, 1912.
Frederick Forchheimer, M.D., died June 1, 1913.
Louis Kolipinski, M.D., died December 14, 1914.
Charles E. Woodruff, A.M., M.D., died June 13, 1915.
Peter Brynberg Porter, A.M., M.D., died August 5, 1915.
Henry L. Elsner, M.D., died February 17, 1916.
Julius H. Eichberg, M.D., died November 2, 1916.
George Ben Johnston, M.D., died December 20, 1916.
Heinrich Stern, M.D., died January 30, 1918.
Jacob Friedman, M.D., died April 13, 1918.
Robert Coleman Kemp, M.D., died Oct. 23, 1918.

## PAPERS READ AT THE 20th ANNUAL MEETING

Water Metabolism of the Organism in Its Relation to the Digestive Secretions ..... Dr. John C. Hemmeter
*Medical Record* 5-20-1920

Peripheral Irritations and Remote Results..... Dr. Robert T. Morris
*Medical Record* 9-20-1919

Lipo-Vaccines..... Dr. A. Parker Hitchens
*Medical Record* 10-25-1919

Organo-Therapy in Certain Diseases and Conditions of Childhood
Dr. Bosworth McCready
*Medical Record* 9-27-1919

The Present Aspects of Endocrinology..... Dr. A. A. Lescohier
*Medical Record* 9-27-1919

The Medical Treatment of Goitre..... Dr. Granville M. Ryan
*Medical Record* 9-27-1919

The Non-Surgical Treatment of Goitrous Disorders. Dr. C. E. De M. Sajous
*Medical Record* 9-27-1919

The Present Status of Prophylactic Vaccination Against Influenza
Dr. F. E. Stewart
*Medical Record* 10-25-1919

Influenza in the Military Camps..... Lt. Colonel M. Jackson, M.D.
*Medical Record* 10-25-1919

Treatment of Influenza and the Pneumonias Incident Thereto
Dr. Jacob Diner
*Medical Record* 10-25-1919

The General Treatment of Influenza..... Dr. Noble P. Barnes
*Medical Record* 10-25-1919

The Control of Epidemic Influenza in a Large Institution
Dr. Horatio C. Wood, Jr.
*Medical Record* 10-25-1919

Angina Pectoris ..... Dr. H. C. Gordinier
*Medical Record* 10-4-1919

Auscultatory Percussion in the Diagnosis of Cardiac Lesions
DR. W. F. MILROY
*Medical Record* 10-4-1919

Therapeutic Problems in Pulmonary Tuberculosis with Disturbances of the Cardio-Vascular System.....DR. ERNEST ZUEBLIN
*Medical Record* 10-4-1919

Rest in Tuberculosis.....DR. FRANCIS M. POTTENGER
*Medical Record* 10-4-1919

The Present Day Teaching of Therapeutics.....DR. SPENCER L. DAWES
*Medical Record* 10-18-1919

The Therapeusis of Aspido-Sperma.....DR. REYNOLD WEBB WILCOX
*Medical Record* 10-25-1919

The Proportionate Dose of Quinine Required to Produce the Same Results in Treating Malarias in Children of Different Ages as in Adults. Illustrated by Lantern Slides.
DR. C. C. BASS—*Southern Medical Journal*

Questions in Relation to the Treatment of Peripheral Nerve Injuries .....DR. W. WAYNE BABCOCK
*Medical Record* 10-18-1919

## OBITUARY OF ROBERT COLEMAN KEMP, M.D.

Dr. Reynold Webb Wilcox read the following: "Dr. Kemp was born in 1865, entered Columbia University from which he was graduated at Bachelor of Arts in 1885 and Doctor of Medicine in 1889. During his college days he was noted as an expert on the bicycle and as the writer of many Columbia songs of enduring value. After graduation he served upon the surgical house staff of Roosevelt Hospital. Early in his medical career he became associated with the late Prof. William Hanna Thomson, and decided to limit his practice to diseases of the digestive tract. Shortly after this decision he was appointed Professor of Stomach and Intestinal Diseases at the Fordham University Medical School, and was a successful teacher in his department of medicine until his death, which occurred on Dec. 23, 1918. He was always interested in research and at one time carried on investigations upon shock, while his later work laid the foundation for important advances in the treatment of the diseases of digestion and metabolism. He also devised several methods and instruments useful in the diagnosis and treatment of diseases of the digestive system. He was an acceptable speaker at the medical societies because he always had a message of importance which was based upon a critical study of the literature, careful research in the laboratory, and painstaking clinical observation.

"He was visiting physician in his department to various hospitals and consulting physician (gastro-intestinal diseases) to the Manhattan State Hospital. He was a member of the various local, State and national medical associations. He was Fellow of the New York Academy of Medicine, member of the Medical Association of the Greater City of New York, of the American Therapeutic Society, of the American Urological Association, and of the American Gastro-Enterological Association. Through his own merits he acquired a large and lucrative practice in his department of internal medicine. The results of his reading, investigation, and clinical observation, were the foundation of his monumental work on the diseases of the stomach, intestines, and pancreas, which immediately won the approval of the profession, and of which the third edition was issued shortly before his death.

"Dr. Kemp as a consultant was respected for the accuracy and therapeutic value of his opinions, as an author for recording the real status of his chosen subject—always giving credit to other workers—as a visiting physician to the wards of humanity for his sympathetic kindness in directing their treatment.

"His home life was ideal, his public services of real value to the world, and his death leaves a void not to be easily filled. Those who knew him well recognized in him not only a great scientist and a distinguished exponent of internal medicine, but an upright, just, and lovable man."

The society then passed into scientific session. Dr. Thomas F. Reilly of New York took the chair during the delivery of the president's address.

# THERAPEUTICS AND GASTROINTESTINAL DISORDERS*

By DOUGLAS VANDERHOOF, A.M., M.D.
Richmond, Va.
Professor of Medicine in the Medical College of Virgina

In the pleasant task of addressing you today, I have chosen as my subject the relation of therapeutics to gastrointestinal disorders. As in every correct application of therapeutic endeavor, however, the consideration of this broad field involves primarily an analysis of the causative factors and a correct interpretation of their clinical manifestations.

The term "indigestion," so frequently applied by the patient to a great variety of ailments, is becoming obsolete in medical literature. This is due, of course, to the fact that indigestion is in most instances only a symptom and not a disease. Yet indigestion is one of the most frequent complaints that brings the patient to the doctor. For this reason, I shall make free use of this term to designate the complaint of patients with symptoms referable to the stomach, bowels, and abdomen in general.

It is distinctly unfortunate, as I have emphasized in a previous address,[1] that the physician who is particularly interested in gastrointestinal disorders soon becomes regarded as a "stomach specialist." Such a designation is infelicitous in that it implies too narrow and incomprehensive a field of work. A case of "long-standing indigestion" will often require all the ingenuity of a competent internist and his Roentgenologist in the process of diagnosis, to be supplemented in its treatment by the surgeon, orthopedist, dentist, oculist, or neurologist.

*The Causes of Indigestion.*—The attempt to classify the causes of indigestion has been a matter of some difficulty in the past. As a result, a purely symptomatic nomenclature has obtained, which still appears in most textbooks on the subject. Several years ago I made a clinical study[2] based on the histories of one thousand consecutive private patients who presented themselves for the relief of chronic or recurring indigestion. The series embraced only those patients whose chief complaint was attributed to some disturbance of digestion, such as "stomach trouble," dyspepsia, abdominal pain, flatulence, vomiting, etc., and entirely excluded patients complaining of other symptoms who were found on examination to have some lesion of the gastrointestinal tract.

*President's address.

The result of this study was so interesting that I have recently added an additional one thousand cases and have tabulated the clinical diagnoses in these two thousand consecutive patients as shown in the accompanying chart.

CASES OF "INDIGESTION"—ANALYSIS OF 2,000 CASES

| | Cases | Per Cent |
|---|---|---|
| 1. Chronic appendicitis | 436 | 21.8 |
| 2. Chronic Cholecystitis | 224 | 11.2 |
| 3. Neuroses | 218 | 10.9 |
| 4. Peptic ulcer | 206 | 10.3 |
| 5. Kidneys, affections of | 137 | 6.8 |
| 6. Achylia gastrica (uncomplicated) | 81 | 4.0 |
| 7. Visceroptosis | 69 | 3.4 |
| 8. Lungs, affections of | 60 | 3.0 |
| 9. Heart, affections of | 50 | 2.5 |
| 10. Cancer of stomach | 46 | 2.3 |
| 11. Blood and ductless glands, affections of | 44 | 2.2 |
| 12. Enterospasm (mucous colitis) | 40 | 2.0 |
| 13 Peritoneal adhesions | 38 | 1.9 |
| 14. Female pelvic organs, affections of | 35 | 1.7 |
| 15. Eyes, affections of | 32 | 1.6 |
| 16. Migraine | 26 | 1.3 |
| 17. Central nervous system, organic disease of | 22 | 1.3 |
| 18. Cancer of intestine | 21 | 1.0 |
| 19. Infectious disease | 19 | 0.9 |
| 20. Liver, affections of | 18 | 0.9 |
| 21. Ears, affections of | 16 | 0.8 |
| 22. Enterogenous toxemia | 11 | 0.5 |
| 23. Miscellaneous conditions | 114 | 5.7 |
| 24. Diagnosis not made | 37 | 1.8 |

Each patient in this series has received thorough study embracing a careful history, complete physical examination, and the necessary laboratory analyses, including as a routine one or more gastric analyses, urine examination, and differential blood count, with hemoglobin determination. In the second half of the series the fractional method of gastric analysis has been employed and routine Wassermann tests of the blood serum have been done. Advantage has been taken of skillful x-ray studies, and much helpful advice has been secured in free and unconstraind consultations with my surgical colleagues, in whose operating rooms I have seen many of these patients treated surgically.

Of course, I am aware that the value of such a tabulation of diagnoses is open to question, and that it is dependent upon the constructive reasoning that supplements a careful and complete study of each individual patient. In addition to the possible margin of error, certain patients presented more than one lesion that might have acted as a

reflex cause of indigestion. In such instances I have tabulated, according to my discretion, the one that seemed most likely to be responsible.

The deduction to be drawn from this table, granting that the diagnoses are essentially correct, are most instructive. These figures show that chronic appendicitis heads the list of causes of chronic or recurring indigestion, and accounts for about one-fifth of all cases. In like manner, chronic inflammation of the appendix or of the gallbladder is responsible for one out of every three instances (33 per cent.) of chronic or recurring indigestion. Approximately 10 per cent. of cases are due to peptic ulcer, while functional disturbances, and affections of the kidneys and heart, each account for another 10 per cent. Cancer of the stomach and intestines shows an incidence of less than four per cent. A word of explanation is in order regarding the frequency of achylia cases (four per cent.). Gastric anacidity is found in about one-sixth of all patients subjected to gastric analysis as shown by me in a previous article. Certain of my achylia cases do not appear in the table because, as is so often the case, the patients did not complain of indigestion, but of other symptoms, such as weakness, nervousness, etc., or had an unexplained anemia; while in many other instances of achylia the cause of the patient's trouble was found to be cholecystitis, malignant disease, etc., and so indexed. The four per cent. incidence refers to "dyspeptics" with uncomplicated gastric anacidity.

Included under miscellaneous conditions in the table are such diseases as pellagra, amebic dysentery and malaria, together with focal infections of the tonsils and teeth, and instances of cyclic vomiting, intestinal parasites, cardiospasm, diverticculitis, peritoneal tuberculosis, cancer of pancreas or esophagus, retroperitoneal sarcoma, hypertrophic spondylitis, etc.

*The Symptoms of Indigestion.*—The chief symptoms presented by the patient with chronic or recurring indigestion are comparatively few and limited. They may be conveniently discussed under the following heads:

1. Loss of Appetite: Distaste for food or a disinclination to eat is a most important sign of impaired health in animals (dogs, horses, etc.), as well as in infants and young children, and the return of appetite is an indication of restoration of health. In human adults loss of appetite is also significant, but its importance as a symptom is diminished by the fact that man resorts to so many artificial aids to his appetite. Carlson has shown that there may be absence of the normal gastric hunger contractions even in cases where no organic lesion in the stomach can be demonstrated.

Anorexia indicates that there is something wrong in the economy,

as James Mackenzie expresses it, or is an indication that all is not well. It arises from a variety of unrelated causes and is not incompatible with a perfectly good digestion. Examination may reveal the cause and the appetite return when the cause is removed.

2. Coated Tongue: As a symptom of indigestion, the coated tongue gives no evidence of real value, and its appearance is certainly subordinate in importance to the condition of the teeth, tonsils, and pharyngeal wall. The tongue is in no sense the mirror of the stomach and there is no direct relation between the coating of the tongue and affections of the stomach. I know of only one condition of the tongue from which any forecast may be made of the gastric secretions, and that is the bald, red, and glazed tongue often seen in cases of gastric anacidity.

As a matter of interest, I made a review[4] several years ago of the histories of 1500 consecutive patients on whom gastric analyses were made and noted the accompanying description of the tongue. The findings were tabulated as follows:

| Gastric Analysis | Tongue Clean, per Cent. | Tongue Coated, per Cent. |
|---|---|---|
| Anacidity | 35.0 | 65.0 |
| Subacidity | 35.9 | 64.1 |
| Normacidity | 35.0 | 65.0 |
| Hyperacidity | 27.3 | 72.7 |

The interesting fact is thus brought out that the proportion of clean and coated tongues is independent of the state of the gastric juices. The slightly higher percentage of coated tongues in hyperacidity cases probably has no significance, and it is believed that a larger series of patients would show about the same proportion of coated tongues in both hypoacidity and hyperacidity.

Investigations by Mueller (1898) and Fuchs (1900) showed that 62 per cent. of apparently healthy people had coated tongues. Hence the further interesting fact is elicited that the appearance of the tongue in patients requiring gastric study is not essentially different from that in healthy individuals.

The chief causes of a pronounced coating of the tongue are three: (*a*) Nasal obstruction with mouth breathing. The mouth is not intended as a respiratory passage, and any interference with the normal manner of breathing brings about an artificial condition of which one symptom is the furred or coated tongue. Under this cause falls the fever patient and also the habitual smoker.

(*b*) Absence of friction, as noted in patients on liquid diet, etc. The posterior third of the tongue is constantly found coated in many normal individuals, and this is attributed by Mackenzie to the fact that in these

cases the palate is high and arched so that the tongue does not come into contact with the roof of the mouth.

(*c*) Perversion of salivary secretion. With overaction of the submaxillary and sublingual glands, the secretions of the mouth are thick and mucilaginous, whereas the parotid saliva is thin and watery. This perversion of the salivary secretions, which I have explained in detail in the article referred to, is probably the most common cause of coated tongue in neurotic individuals.

3. Nausea and Vomiting: As a symptom of chronic stomach affections, nausea and vomiting are relatively infrequent and of very varied significance. These two symptoms occur under the following diversified conditions:

(*a*) Toxic states; as seen at the onset of infectious diseases, in pregnancy, migraine, hyperthyroidism, acidosis, catarrhal juandice, etc.

(*b*) Reflex disturbances from the eyes, internal ear, pain and emotions.

(*c*) Pharyngeal irritation, seen in the morning vomiting of alcoholics and smokers, and especially in patients with pulmonary tuberculosis.

(*d*) Habit vomiting, seen in individuals who have acquired the trick of emptying the stomach on the slightest provocation.

(*e*) Brain and spinal cord lesions, such as tumors, injuries, tabetic crises, etc.

(*f*) Gastrointestinal diseases. These are comparatively infrequent causes of nausea and vomiting except in instances of pyloric spasm or stenosis, intestinal obstruction, and acute inflammatory conditions within the abdomen.

Vomiting of blood, pure and in quantity, almost always indicates either peptic ulcer or some obstruction of the portal circulation with esophageal or gastric varices.

4. Pyrosis and Sour Stomach: In discussing these symptoms we must remember that the normal stomach content is exceedingly sour. The consciousness of this sourness on the part of the patient indicates pylorospasm with or without regurgitation into the esophagus. Hyperacidity alone is not the cause of "heartburn" and "sour stomach," as it can be proven that the mucous membrane of the stomach is insensitive to greatly increased amounts of hydrochloric acid. Pyrosis is not uncommon in achylia gastrica and has been complained of in 17 per cent. of my anacidity cases. While the cause is obscure, I am inclined to attribute it to the accompanying gastritis. It is relieved by the administration of full doses of hydrochloric acid with the meals.

5. Flatulence: One of the most common complaints of patients

suffering from indigestion is belching or eructation of gas. These patients frequently say that everything they eat "turns to gas," and they occasionally volunteer the information that they are suffering from "*gas*tritis"! They generally believe that the condition is due to fermentation of food in the stomach and not infrequently they have been treated on the basis of such an occurrence.

In the light of the many investigations that have been made in the study of flatulence, it has been abundantly shown that most of the gas in such cases is really atmospheric air that has been swallowed. Fermentation may be an added factor in instances of pronounced stasis, but can give rise to only a definite and small quantity of gas. A third factor is the likely possibility of so-called "alimentary respiration" with the actual secretion of carbon dioxide by the gastric and intestinal mucosa. An excellent discussion of this subject in general is to be found in a recent article of Kantor[5] to which is added an extensive bibliography.

Air-swallowing, or aerophagia, is seen in its most striking form in hysterical subjects. In such cases enormous volumes of air may be expelled. Instances are on record of patients who have belched over 5,000 times in 24 hours, and the amount of air eructated has been measured and found to exceed 200 liters. It is evident, in examples of this kind, that the quantity of gas expelled is many times in excess of that which could possibly be produced by any conceivable process of fermentation. Furthermore, the gas eructated in such cases has been collected and analyzed and shown to consist of oxygen and nitrogen in about the proportion found in atmospheric air, with the admixture of a small quantity of carbon dioxide. This latter gas may represent an actual secretion of the gastric mucosa or may arise in part from the decomposition of the carbonates in the food or in the swallowed saliva. Carbon dioxide is produced in quantity, of course, when a patient with a normally acid gastric juice takes a full dose of bicarbonate of soda.

Aerophagia is entirely independent of the character of the gastric secretions, and may occur as a pure neurosis, or may be a symptom accompying many and varied organic diseases. Some years ago I showed that air-swallowing occurs relatively as frequently in patients with gastric subacidity as in those with an excess of hydrochloric acid, and that it is just as much a feature of organic disease as purely functional ones.[6]

To the unfortunate patient afflicted with flatulency, the condition is real and apt to be distressing. To the physician making the diagnosis, flatulency is a symptom of minor importance. The relief of the condition demands the removal of the cause, whether it be gallstones, an error of refraction, or simply a bad habit.

6. The Significance of Mucus: The secretion of increased amounts

of mucus by the stomach, or by any mucous membrane in the body, is frequently attributed, in a most complacent manner, to catarrh. This unfortunate term is defined (Dorland) as an inflammation of a mucous membrane with a free discharge. According to the newer gastrointestinal studies, the production of increased quantities of mucus does not indicate in any way an inflammatory condition of the mucosa but rather a nicely adapted protective measure.

As an experimental proof one can best refer to one of the classic experiments of Pawlow, which is summed up in the following quotation:

"When powerfully acting substances, such as absolute alcohol, a 0.2 per cent. sublimate solution, a 10 per cent. solution of nitrate of silver, or a strong emulsion of oil of mustard, were introduced for a few minutes into the stomach (of the experimental animal), they produced a more or less considerable, indeed, in many cases an enormous secretion of mucus. One might think this was a serious pathological condition, an acute mucous catarrh. Is it, however, a condition of disease? In extreme cases, more than one hundred times the normal amount of mucus was secreted by the irritated surface. At times, only mucus instead of juice was obtained during the whole period of secretion, and yet I ask again, is it a morbid state? Often, after the lapse of an hour or two, the more or less copious secretion of mucus, which immediately appeared upon the application of the irritating substance, had wholly exhausted itself; or an enormous flow of mucus, which on the day of the experiment had completely suppressed the normal secretion of gastric juice, may, on the next day, to one's utter astonishment, have disappeared without leaving a trace behind. The contrast between the intensity of the phenomenon and its short duration is really striking. One cannot resist the idea that in the cases described no morbid condition had as yet been established, but rather that the pathogenic influences had been successfully battled with and conquered before our eyes. Has not the true physiological function of the surface epithelium of the stomach been here revealed—a function of which we could form no adequate conception in the normal course of affairs? By virtue of its wonderful power of secretion a large quantity of mucous fluid is poured out which dilutes the noxious substance, or forms chemical combinations with it, and drives it away at the same time from the stomach wall. The surface epithelium thus wards off the danger which threatens the more important elements of the mucous membrane beneath. That this explanation is correct is also shown by the fact that the peptic glands remain absolutely at rest, in striking contrast to the extreme activity of the surface epithelium."

Mucus in the gastric contents is observed most frequently in cer-

tain cases of achylia and in instances of alcoholism. The daily introduction of food into the achylous stomach, where it remains unchanged and undigested until it passes into the duodenum, would eventually prove distinctly irritating to the gastric mucosa did it not defend itself by the outpouring of mucus. In a similar way, the drinking of inordinate amounts of whisky provokes an abundant flow of mucus in the stomach, thus giving rise to the clinical picture of so-called alcoholic gastritis.

Mucus in the stools does not denote inflammation but rather a protective reaction against irritants, chiefly cathartics. It is associated almost invariably with a spastic contraction of the intestinal walls. So-called mucous colitis is not in any sense an inflammatory lesion but in reality a severe spastic constipation, or enterospasm, often amenable to observation by the sigmoidoscope or by x-ray studies of the colon. The first essential in the treatment of enterospasm, as I have pointed out elsewhere, is rest for the bowels. This can be secured only by the absolute discontinuance of strong purgatives and all forms of intestinal irrigations. When this is supplemented by a proper full diet, plus belladonna and mineral oil, it is surprising how quickly the condition can be controlled.

7. Visceral Pain: The cause of pain in visceral disease is too large, and perhaps too controversial, a subject to discuss here. If, however, one follows the teaching of Mackenzie and others, and appreciates the fact that effective stimulation of any part of a nerve fiber, from the periphery to the brain, elicits prompt evidence of its peculiar function—*e.g.* the optic nerve, the auditory nerve, etc.—the cause of pain in visceral disease is not so difficult to understand.

"In the normal processes of life a succession of stimuli is continually passing from the viscera, by the afferent nerves, to the spinal cord. Here they react upon the efferent nerves which supply muscles, blood-vessels and other structures. Under conditions of health these processes are so conducted that they give rise to no appreciable sensation. If, however, on account of a morbid state in any viscus, an increased stimulus passes by the afferent nerves to the spinal cord, this abnormal stimulus may be sufficient to affect neighboring nerve cells. These cells then react according to their function, a sensory cell by producing pain, a motor cell by the contraction of certain muscles, a secretory nerve by increased flow of its peculiar secretion, and so forth."[9]

Then again, it has been shown that in visceral disease certain areas in the spinal cord become so irritable that stimuli from the viscera give rise to an exaggerated response. "The irritable focus in the cord is of great frequency in stomach affections. When pain occurs after food it must not be assumed that there is an inflammation of the mucous

membrane, or that the stomach itself is hypersensitive. The ingestion of food under normal circumstances is accompanied by reflex processes which are not perceived, and pain merely indicates that there is an irritable focus in the cord through which these reflex processes pass. The lesion inducing the irritable focus in the cord may not necessarily be a stomach lesion at all, but may arise from a neighboring organ whose reflex center in the spinal cord is in close proximity to that of the stomach." Thus in gallstone colic, or in acute inflammation of the appendix, the afferent stimulus may be so violent as to invade the stomach area in the cord, and in chronic inflammations of these same organs this invasion of the area in the cord gives rise to the various train of symptoms referred so constantly to the stomach.

*Treatment of Indigestion.*—As stated in my introductory remarks, the term "indigestion" is a broad one and covers a variety of conditions. Throughout this article I have used it intentionally to include the complaints of patients referable to the stomach and intestines.

The first thing to consider in dealing with indigestion is that we are called upon to treat a symptom, *e.g.* pain, vomiting, flatulence, etc. To be successful, however, we must not treat the symptom as such, but find and eradicate the underlying cause. Simply relieving the symptoms rarely cures chronic or recurring indigestion. The cause of the symptoms must be determined and explained in a proper way, and it should be realized that it is not what one eats that gives rise to indigestion but the state of the gastric nerves when one eats. The popular idea of restricting the diet of every patient with indigestion is not only a fallacy, but may be largely responsible for the continuation of the symptoms. Drugs of course, have their place (1) in relieving symptoms, as witness the value of belladonna and alkalies in pylorospasm, and (2) in removing the cause, *e.g.* digitalis in chronic passive congestion of the stomach and liver in myocardial insufficiency. Psychotherapy cures some cases, proper eye-glasses others, glandular therapy still others. The important part played by competent surgery, when based on proper study and interpretation of symptoms, is one of the greatest advances of recent years in the treatment of many gastrointestinal disorders.

In conclusion, may I again call attention to the table in the early part of this article, wherein are compiled the more common causes of chronic or recurring indigestion in the order of their frequency. A brief consideration of such a tabulation suggests at once the treatment to be adopted in most instances.

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# 21st ANNUAL MEETING

## College of Physicians

## Philadelphia, Pa., May 7th and 8th, 1920

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*Medical Record* 9-18-1920

Some Aspects of Hyperchlorhydria with Special Reference to Treatment
Dr. Julius Friedenwald
*Medical Record* 9-18-1920

The Control of Hyperchlorhydria by Cholecysto-Gastrostomy
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Report of 1,000 Heart Patients Subjected to Complete Examination, with Important Therapeutic Results .....Dr. Louis F. Bishop
*Medical Record* 9-25-1920

Glandular Extracts in Cardio-Vascular Disease
Dr. Thomas E. Satterthwaite
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*Medical Record* 9-11-1920

The Therapeutics of Benzosulphinide.....Dr. Reynold Webb Wilcox
*Medical Record* 10-9-1920

# OBITUARY

## HORATIO C. WOOD, M.D.

### AN APPRECIATION.

By Henry Beates, Jr., M.D., Sc.D.,
Philadelphia

By the death of Prof. Horatio C. Wood the medical profession and mankind in general have suffered an irreparable loss. His life was an example of sincerity of purpose, diligence, honest endeavor, and justice, and an exceptionally powerful influence for the uplift, growth, and development of those sciences with which he was identified. Endowed with an unusual mind, and insatiable in the acquisition of knowledge, the ever conspicuous power and faculty of learning were demonstrative of his great intellect.

Indefatigable as an investigator, utilization of time and opportunity found him ever active in the study and solution of problems presented by the various natural sciences to which his life was dedicated.

The eagerness with which he engaged in study was a conspicuous characteristic, and illustrated by the following incident that occurred when a mere youth: Visiting the Philadelphia Academy of Natural Sciences and standing before a locked cabinet containing specimens in which he was deeply interested, and being unable to handle and examine them, his disappointment found expression in tears. The great Leidy passing by, and noticing the distress of the youthful Wood, inquired the cause. Being informed, and doubtless recognizing the impulses of genius, he had the cabinet unlocked and the specimens placed at the student's disposal.

Dr. Wood was an enthusiastic student of botany. In 1860, when but 19 years of age he presented his first scientific paper, entitled "Contributions to the Carboniferous Flora of the United States." From then until 1873 fourteen papers, each of which was an authoritative classic, appeared in the Proceedings of the Academy of Natural Sciences, the American Philosophical Society, the Queckett Microscopical Club Journal, the Smithsonian Institute, and in the *American Journal of Science*. In 1872 the Smithsonian Institute published Dr. Wood's monograph, "The Fresh-Water Algae of North America." This 270-pp. quarto contained 19 colored and 2 uncolored plates, prepared from 360 original microscopic drawings which, for accuracy of detail and per-

fection, are unsurpassed. It remained the authoritative work on this subject for 25 years.

Demonstrative of Dr. Wood's phenomenaliy acute powers of observation and consequent ability to recognize and discover new species, the following botanical papers may be mentioned: "Life History of Some Siphonaceous Fresh-Water Algae," "Manner in Which *Schizomeris leibleinii* Produces Its Zoospores, and New Species of Desmids," "New Species of the Genus, Sirosiphon, *S. lignicola, S. phloiophilum, S. disjunctum.*"

Entomology also engaged his attention during these years, and his achievements in this branch of science culminated in fourteen papers characterized by that thoroughness and masterful research which stamped each as an authoritative contribution and an acquisition of knowledge. Of these studies, which want of time prevents naming, that entitled "The Myriapoda of North America" was published in the American Philosophical Society Transactions in 1865. It was a brochure of 112 pages, with 61 figures in the text and 3 plates. The drawing, true to nature, were exponent of his skill. The excellence and reliability of his work was recognized by Louis Agassiz, who in 1865 headed a large naturalizing expedition to Brazil, and, after his return, wrote the following letter to Dr. Wood:

DEAR SIR:

While in Brazil I have collected a good many myriapods in every part of the empire visited, and I will glady put the whole at your service as soon as the specimens can be picked out, but I cannot say how soon this will be possible, as I cannot make a beginning with the arrangement of my collection before I can secure the means of buying about 5000 gallons of alcohol to carry the work through.

Very Truly yours,

AGASSIZ.

Dr. H. C. Wood.

Dr. Wood was an indefatigable worker. He would frequently concentrate his mind upon the subject in hand for 30 consecutive hours; then relax and indulge in an uninterrupted sleep of from 12 to 18 hours, when his insatiable thirst for knowledge found him again active in the pursuit of investigation and discovery, with that intensity of interest and painstaking care in observing the minutest details which crowned his labors with phenomenal success.

Profound learning necessarily established a high plane from which to observe conventional standards of achievement, and enabled Dr. Wood to enter his chosen profession of medicine with a mind exceptionally well informed, and an intellect of superior power.

As professor of botany in the Auxiliary Medical Course of the

University of Pennsylvania, his ability as a teacher was highly cultivated, and his occupancy of the Chair of Materia Medica and Therapeutics in the major faculty of medicine constituted one of the strongest and most influential chairs of the then famous center of medical education. He was a brilliant and impressive lecturer and a teacher of great renown.

Dr. Wood's career in the natural sciences rendered him extremely alert in recognizing the inevitable consequences of cause and effect. He was painfully conscious of the imperfections and limitations of empirical medicine, and the measure thereof found expression in the fearless manner in which, then almost single handed, he entered the arena in a struggle having for its aim the establishing of physiologic or rational medicine upon a firm and scientific basis. With an open mind, ever alert to recognize and acknowledge truth, he did not belittle the knowledge of means to end that empirical medicine had established, but sought to add thereto elucidation and explanation. His sincere willingness to entertain and accept demonstration of mistake or error was parallel with his eagerness and desire to guide and instruct and guard against error wherever and whenever encountered, and the measure of his true greatness. To Professor Wood belongs the honor of having been a pioneer in establishing the Epoch of Rational Medicine. The courage of conviction that found him alone championing rational medicine, *i.e.* therapeusis based upon knowledge and logical conclusion, was conditioned upon the recognition of the defects of empirical medicine. From the first edition of his epoch-making treatise on Therapeutics published in 1874, and antedating that of Lauder Brunton by 10 years, of which 14 editions were printed, and have served as a model for text books on Therapeutics in European countries, as well as in the United States, the following quotations from the preface serve to emphasize the firm foundation upon which he stood:

> There are a number of excellent treatises upon Materia Medica and Therapeutics, yet in various attempts at original research, as well as in the ward and lecture room of the hospital I have keenly felt the want *of something more.* The old and tried method in therapeutics is that of empiricism, or if the term sounds harsh, of clinical experience. The best possible development of this plan of investigation is to be found in a close and careful analysis of cases before and after the administration of a remedy, and if the results be favorable the continued use of the drug in similar cases. That very much has been thus accomplished it were folly to deny. Therapeutics developed in this manner cannot rest, however, upon a secure foundation. Looking at the revolutions and contradictions of the past, listening to the therapeutic babel of the present, is it a wonder that men should take refuge in nihilism, and like the lotus eaters, dream that all alike is folly—that rest, and quiet, and calm are the only human fruition? A primary knowledge of the end to be accomplished and a secondary acquaintance with the instruments, are a necessity for human effort, and until the

sway of this law is acknowledged by physicians, medicine can never rise from the position of an empirical art to the dignity of applied science. The work of the therapeutist is with the second portion of the law. Evidently it is his special province to find out what are the means at his command, what the *individual drugs in use do when put into a human system.*. Thus did the champion and pioneer of Rational Medcine enter the arena of controversy and withstand the attacks of relatively ignorant and emotional anatgonists who sought by all means available, social, financial, and political, to prevent scientific investigation, and the establishment of the Era of Rational Medicine.

Animal experimentation was a *sine qua non* which was most bitterly opposed. No less an authority (an authority, however, in another sphere, be it remarked) than the famous Niemeyer asserted that experiments made with medicaments upon lower animals, or upon healthy human beings have, as yet, been of no direct service to our means of treating disease, and that a continuance of such experiments gives no prospect of such service. The antagonists asserted that medicines did not affect lower animals as they did human beings. Apparently the contention was well taken, but Dr. Wood demonstrated that while apparently this was true, in reality it was erroneous, and a misinterpretation. He proved that while it required as much morphine to kill a pigeon of a pound weight as to destroy a man, it was not a different action, but on the contrary, an identical one, the seemingly different effects being dependent upon varied degrees of susceptibility, and that the modus operandi was identical. This physiological law or truth Dr. Wood further demonstrated by a study of atropine. Contrasting an animal which may be exceedingly sensitive to the spinal action of atropine with one in which it exerts its effects upon the conducting fibers of the nerve trunks, we find it causes convulsion in one and paralysis in the other. This law makes understandable why so many drugs seemingly exert an antagonistic action. Dr. Wood, by conclusively demonstrating that degree and quality are *two separate and distinct things, and should never be confounded,* successfully combated the efforts of ignorance and emotionalism to make it a crime to pursue scientific research. What may be properly designated as the magnum opus of Wood, the institution of an epoch in medicine characterized by the relinquishment of the empirical and the adoption of the rational, and of establishing an era conspicuous for achievements in preventive as well as curative medicine is sufficient to place his name side by side with those of the immortal Hippocrates, Galen, Sydenham, Hunter, Lister, Laennac, Jenner, Pasteur, and Koch.

In 1810 Majendie, studying the effects of nux vomica, recognized the vital importance of knowing how medicines affected the human system, but to Prof. Horatio C. Wood belongs the credit of having

brought to the recognition of the medical world the necessity of adopting physiological or rational medicine as the one essential means of acquiring knowledge and skill and art in the prevention and treatment of disease upon which humanity depends.

Dr. Wood consecrated himself to medicine. In 1869 he made his famous experiment upon himself with American grown cannabis. The following year his first paper on the "Physiological Action of Drugs" was published in the *American Journal of the Medical Sciences*. His studies of the action of veratrum viride led to its general adoption by clinicians. In 1871 Dr. Wood's papers treating of the physiological action of amyl nitrite were published. Two years previously Lauder Brunton published his paper which set forth the value of amyl nitrite in angina pectoris, but the contribution of Dr. Wood was the first description of the physiological action of the drug upon the nervous system. His investigations of chloroform, ether, and other anesthetics, are so well known that mention only is necessary. These results were published in 1890, and the following year found him honored with being selected to make the principal address before the general session of the International Medical Congress at Berlin. These studies have probably been responsible, more than the work of any other scientist, for the general adoption of ether as an anesthetic by the entire surgical world. It was while pursuing the studies of anesthetics and the treatment of their toxic effects that Dr. Wood discovered the value of strychnine as a respiratory stimulant, and its importance in averting threatened death.

Of 5,000 scientists present at the Berlin Congress the Duke of Bavaria, a physician, selected and entertained 25 who were noted for exceptional achievements. Of these Professor Wood was one, and when about to be seated the duke, removing his crown, placed it upon Dr. Wood's head, and further honored him by requesting him to occupy the chair pro tem. Thus Professor Wood was a Duke of Bavaria for almost an hour.

In 1903 Dr. Wood represented the United States Government at the International Conference, held in Brussels for the purpose of unifying the more important preparations of the various pharmacopeias. Early in its session the conference became so involved in acrimonious dispute as to the proper percentage of alcohol to be used in making tinctures that the whole usefulness of the meeting was seriously threatened. His strong personality and recognized advocacy of justice and right enabled him to convince the delegates of the foolishness of quibbling over minor details, and they finally adopted the present regulation of 10 per cent. tincture and various other standards which are recognized by the pharmacopeias of practically all civilized nations. This busy practitioner,

teacher, investigator, and author published a text-book on nervous diseases and their diagnosis in 1887, and of the 240 medical papers, each one of which was a classic, and an addition to the knowledge of the science and art of medicine, the treatise on thermic fever, or sunstroke, has especial value. Published in 1872, it was accorded the Boylston prize. That this work has contributed to the saving of thousands of lives annually is an evidence of one of the great services this man of genius has accorded to humanity.

His investigations of fever culminated in a work of 250 pages, which was published by the Smithsonian Institute in 1880. It is a monument to his learning and a most valuable contribution to medical science. Dr. Wood discovered the alkaloid hyocine while studying the effects of hyoscyamine, and in 1885 demonstrated its value for certain nervous diseases.

His researches in experimental pharmacology, physiology, and pathology embody more than fifty contributions of knowledge to the science and art of medicine.

Twelve conscientiously elaborated subjects of medical jurisprudence and toxicology which were, as all of his works, instructive and of great practical value, were contributed from the years 1873 to 1899.

As a clinician, his studies of pathology, medicine, and therapeutics comprise 139 papers, which for originality and profundity of learning are invaluable. Thirty-six published lectures and addresses appeared in various journals during the years from 1874 and 1900, and extended his beneficial influence throughout the continent.

Nine magazine articles from the year 1872 to 1879 brought to the lay mind information and knowledge which proved of great value in securing popular cooperation with efforts instituted by the profession for the betterment of standards of medical efficiency. In 1875 there appeared in *Lippincott's Magazine* an article contributed by Dr. Wood entitled, "Medical Education in the United States." This paper brought to a crisis the agitation which had been active for many years concerning this matter, which was and is of such vital importance to the profession of medicine, as well as the greatest and highest interests upon which human welfare is conditioned. It caused radical changes in the medical department of the University of Pennsylvania and indirectly compelled other colleges of medicine to reform their curricula. It advocated State board examinations, and was a powerful influence for the establishment of the legal supervision of the qualifications and rights to practice the healing art.

In 1889 Yale University conferred upon Professor Wood the degree LL.D. The occasion was made an opportunity for Dr. Wood to use his

influence in promoting and intensifying interest in higher medical education. The title of his address, "The Medical Profession, the Medical Sects, the Law," emphasized the necessity of demanding for the doctorate men of proper preliminary education, and the administration of an ample curriculum. The too commonly encountered unfitness of clinicians upon whom colleges had conferred the medical degree and the fearful consequences of this, he emphasized by the astounding statement that the horrible disasters of the Johnstown flood were insignificant when compared with those resulting from the illy prepared and unqualified practitioner. So strongly was Dr. Wood convinced of this seriously inadequate but then prevalent system of medical education, that the comparison was unhesitatingly presented to the interested audience with that vehemence which characterized his advocacy of higher ideals.

'Tis the habit of action that individualizes man, and imparts special qualities to his character. That "Nature never rhymes her children nor makes two men alike" is a fact that explains why men of genius constitute a center from which emanate influences for either good or evil that powerfully modify the lives of all within their range. That Dr. Wood was keenly alive to this great truth is made manifest by his definition of character. "Character is the established equilibrium existing between the emotional, the intellectual, and the volitional" are his words. To establish and possess that equilibrium is an achievement which few attain. It taxes to the utmost the noblest and best qualities with which a man is endowed, and that Dr. Wood was ever alert to so do was evidenced by his every action. Once, while in conversation, he suddenly stooped down and caught a large roach that was crossing the floor, and holding it in his hand, fondled it. Being asked why, his reply was that to master a baseless dislike of anything harmless was invaluable, and when it caused one to overcome empty prejudices, it contributed to the usefulness of being and did much to give force to one's influence for the betterment of fellow-man.

Dr. Wood was profoundly conscious of the value of time, and as a superficial glance into his active life shows, every moment was advantageously occupied. As an example of untiring and continual work he stands preeminent and the fundamental principles underlying his achievements are well shown by the subject of his inaugural address before the trustees, faculty, and student body of the University of Pennsylvania, when as professor of Materia Medica and Therapeutics his wonderful career in that capacity began. He urged upon every one that a definite object in life be the goal for which to strive, and that substantial progress is conditioned upon a thorough mastery of each involved factor. In that manner by which he had the happy faculty of impressing great

truths upon the minds of his pupils, he drove home these principles by quoting from Mother Goose, how leg over leg the dog got to Dover, and all who were privileged to hear him proclaim how the dream of his life was to become a professor and that by a conscientious mastery of minute and upbuilding details the goal was reached, were doubtless stimulated to emulate the great teacher and strive to do their best.

As Emerson so impressively states, character is the moral order seen through the medium of an individual nature. An individual is an enclosure—time and space, liberty and necessity, truth and thought are left at large no longer. All things exist in the man tinged with the manners of his soul. With what quality is in him he infuses all nature that he can reach, nor does he tend to lose himself in vastness. He animates all he can, and he sees only what he animates. He encloses the world as the patriot does his country as a natural basis for his character and a theater for action. A healthy soul stands with the just and the true as a magnet arranges itself with the pole so that he stands to all beholders like a transparent object betwixt them and the sun, and who so journeys toward the sun journeys toward that person. He is thus the medium of the highest influence to all who are not on the same level. Thus men of character are the conscience of the society to which they belong. To the honor and memory of the great and first president of the American Therapeutic Society may be justly ascribed the consummation of a life conspicuous for moral, intellectual, and physical excellence, the influence of which for betterment activating the thousands emulating his example will continue on and on anon. His life will ever serve as a guide and stimulus for right living, and constitute a power for good in the uplift of humanity as lasting as time.

260 South Sixteenth Street.

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## THE ABANDONMENT OF THERAPEUTICS IN MEDICAL SCHOOLS DUE TO NEGLECT OF ITS CURATIVE SUBDIVISION: PHARMACO-ENDOCRINOLOGY*

By CHARLES E. De M. SAJOUS, M.D., LL.D., Sc.D., F.A.C.P.
Philadelphia.

You will recall that at our last meeting, one of our members, Dr. Spencer L. Dawes, a trained teacher of therapeutics, delivered an address entitled "The Repudiation of Materia Medica and Therapeutics in Modern Medical Teaching," which began with Marc Antony's admonition: "Friends, Romans, Countrymen, lend me your ears: I come to bury

*President's address,

Caesar, not to praise him." I have unfortunately, no classic sentence to convey my meaning so tersely but I might say: "Friends and Fellow Members, I have not come to bury Therapeutics, but to revive it."

Referring you to Dr. Dawe's paper for details,[1] I will merely recall that after recognizing in glowing terms the progress made in almost every branch of medicine, he earnestly deplores the practical abandonment of the teaching of materia medica and therapeutics in our medical schools. "Those who dominate to-day," he said, "require of a graduate two very valuable requisites: they must be able to make a diagnosis and they must know pathology and be able to make an autopsy so as to confirm their diagnosis. But treat disease, cure the sick, relieve pain and suffering—nonsense! What true scientist cares for such rot!" Another fellow member, Hobart A. Hare,[2] has graphically portrayed the evil effects of this attitude of most medical colleges upon the student, the young graduate, the interne, the medical man to whom men and women must entrust their lives and those of their children.

You will agree with me that we should deem it a moral obligation as members of the American Therapeutic Society to protest against any tendency on the part of any of our schools to divert students from their aspiration to serve suffering humanity loyally and honestly as physicians worthy of the name. Yet our obligations involve also the responsibility of inquiring whether there is not some deep underlying cause for this wholesale neglect of therapeutics, and whether it might not be possible to turn the tide.

An unlocated, open seam in the hull of a great ship has sufficed to sink it; personal analysis of the question in the course of seventeen revisions of the entire medical field for an Analytic Cyclopedia has suggested that quite as dangerous a defect exists in therapeutics. To say that there is nothing in this branch of medical science, as does the therapeutic nihilist, is naught else than testimony to his lack of knowledge upon the subject provided palliation of suffering and slowing the destructive trend of disease are deemed the sole objects of medical treatment. But may we compare the *curative* efficiency of our drugs with that of surgery, for instance—or with the wonderful showing of preventive medicine in smallpox, typhoid fever, and other destroyers of humanity?

What I deem the missing factor to be reminds me of Voltaire, the great French cynic, who, by the way, was at heart a religious man. Seeing on all sides churches dedicated to various saints, St. Peter, St. Paul, St. Luke, St. Clement, etc., he concluded that he would depart from the rule by dedicating a noble edifice to the greatest of all divinities, the forgotten One, God Himself. And thus it is with present-day

pharmacology; apart from six or seven specifics and vermifuges, most of which were discovered before experimental therapeutics had seen the light of day, symptomatic treatment, very useful when used intelligently, that is to say when not interfering with Nature's own curative means, is the limit of our efforts. What should be our cardinal and paramount object, however, the cure of disease, as Dr. Dawes puts it, "is not even a secondary matter; it is simply ignored." He critically refers to the multiplicity of cults in the remedial field that have sprung upon all sides. Does this not in itself prove that pharmacology has failed in its avowed aim? Would these cults prosper if therapeutics had held its own with scientific progress in other branches of medical science which have had the preservation of life in view?

College authorities overlook a feature of overwhelming importance in this connection. They are undermining the very existence of medicine as a whole. Graduates will soon begin to realize that untrained in the treatment of disease, their calling will not be compatible with the trust reposed in them by their patients and increasingly abandon the field, leaving it open to the unscrupulous of all shades and kinds.

The salvation of therapeutics will depend, it seems to me, upon the degree of curative efficiency it can be made to attain. Were the pharmacologist to concentrate his efforts upon its main purpose, *the cure of disease, by studying the influence of drugs upon our defensive functions,* he would endow his chosen field with an attribute that would stimulate endeavor on all sides instead of repelling the practitioner, as he now does, with laboratory complexities in which aggressiveness against the pathogenic factor has virtually no place. As Llewellys F. Barker worded it as far back as 1900, "pharmacotherapy is almost moribund;" let *cure* be the paramount aim of pharmacology once for all and its dying embers will be revivified into a bright flame that all medical men will hail as the great white light of their avowed aim.

How can pharmacology meet the needs of so desirable an end?

Over three decades ago, while editing the Annual of the Universal Medical Sciences, I had already realized, as Bichat had said a century before, that drug therapy was "not a science fit for a methodic mind," and, inspired by the doctrine of Confucius, that "undigested knowledge leads to confusion," set to work trying to introduce some order, where chaos already reigned supreme, through the light that clinical medicine, the ductless glands, and other collateral branches might cast upon them.[1]

Two discouraging factors, however, asserted themselves from the start. Even years later, these could be illustrated, by the estimates of well-known observers: Sollmann, our most prominent experimental pharmacologist, for instance, wrote in 1908: "Pharmacology cannot be

classed as an art, nor a science, it can only be classed as a confusion." The same has been said by many concerning the prevailing knowledge of endocrine functions. Thus, Prof. Halsted, of Johns Hopkins, wrote five years ago: "It must be evident to everyone that there reigns the greatest confusion on the subject of the functions of the glands of internal secretion." That such is the case anyone can readily verify today by glancing through the literature on experimental endocrinology. Briefly, two great confusions were available as sources of knowledge to carry out my purpose! This led me to seek for truth independently, *i.e.* irrespective of conclusions previously reached by others, with what experimental and clinical data had been published up to the dawn of the present century. The product of this labor was published as you well know in two large volumes, the first of which appeared at the beginning of 1903.

Those of our fellow members whom, for so many years, I have addressed since then upon endocrinological subjects, well know that my views, particularly those derived from the clinic, often failed to harmonize with those of physiologists and pharmacologists. Beginning with the adrenals, I failed to find in the sick human biped, though anxious to do so, what physiologists saw in their comparatively diminutive and healthy laboratory quadrupeds. I did not find, for instance, that therapeutic doses of adrenalin or suprarenal gland inhibited the functions of the gastrointestinal canal, as physiologists would have us believe; in fact, these agents often had an opposite effect. Nor did I observe the much-talked-of inhibitory action on the pancreas, judging from the intestinal digestive processes. Even the effect on the blood-pressure failed to materialize in practice—only large doses of adrenalin or suprarenal gland or long continued dosage sometimes causing a rise—along, I might add, with effects recalling those of strychnine. Except in distinct hypoadrenia from any cause, where the pressure was low, the supposed blood-pressure raising power of adrenalin upon which the practitioner, in obedience to physiological precepts, had until recently depended two decades, proved misleading. Physiologists of the standing of Moore and Purinton, Hoskins and McClure, Young and Lehmann, and others, have themselves, in fact, proved the fallacy of this view. Indeed, as Walter Timme,[4] a clinician, wrote after an extensive test in camp at Plattsburg, "If there is one thing adrenalin does *not* do it is to produce a rise of blood-pressure.

Yet, although physiologists were themselves finding erroneous the functions they had attributed to the adrenals, Swale Vincent[5] going so far as to state that evidence warranted the belief that these organs had no definite function, they were unconsciously accumulating evidence

sustaining my own views—all fundamental—in their relations to therapeutics. Briefly, their labors have increasingly shown that the functions I had attributed to the adrenals in 1903 and 1907 had stood the test of time.

When I first undertook the study of the adrenals, much evidence, for instance, had been published tending to show that the process of respiration in the lungs was far from being established. This seemed to me to account for the many gaps in our knowledge of pulmonary and metabolic diseases, I had noted in the course of eight of the revisions of the medical field for my Annual of the Universal Medical Sciences. Indeed, the diffusion doctrine of respiration, so sterile as a source of help in the study of disease and therapeutics, and so costly, therefore, in human lives—and still taught, I regret to say—had been severely criticized for decades by physiologists of the first order, Paul Bert, Muller, Bohr, and others, who showed conclusively that the absorption of oxygen from the air in the pulmonary alveoli necessitated in the blood circulating through the lungs some substance capable of actually appropriating this gas. This conclusion was further sustained, as years went by, by Haldane, Lorrain Smith, and Vaughan Harley. Bohr and Henriques[6] concluded that it was presumably "a kind of internal secretion." the nature and source of which, however, remained undetermined. A comprehensive study of the question in all its phases, including a test of my conclusions in over one hundred diseases and nearly fifty drugs, enabled me to point out that the internal secretion sought was that of the adrenals. The adrenal secretion, after entering the vena cava and passing through the right heart, finally reached the pulmonary alveoli with the venous blood. Here I held, it became a part of the hemoglobin, endowing this pigment with its power to take up oxygen from the air and thus converting it into oxyhemoglobin.

This conception has now been sustained by several experimenters. Menten and Crile[7] in 1915, and Menten[8] in 1917, found experimentally that adrenalin, which is present in the venous capillaries of the lungs, was capable of converting hemoglobin into oxyhemoglobin and of carrying on the respiratory process. I had adduced also considerable evidence, both direct and indirect, including some furnished by many physiologists as well as clinicians, that the adrenal secretion influenced general oxidation and metabolism and that it increased the intake of oxygen and the output of carbon dioxide. Recently, again, Tompkins, Sturgis, and Wearn[9] found that intramuscular injections of 8 minims of the 1-1000 solution of adrenalin caused an increase of the air intake, also of the total gaseous metabolism while augmenting the respiratory rate. It has been objected that the proportion of adrenalin secreted

into the blood was too limited to carry on this function. But the adrenal principle, being an oxidizing catalytic enzyme, is not destroyed while carrying on its functions, and *is secreted only to replenish loss* after marked fatigue or unusual excitement—a fact which explains, from my viewpoint, why Cannon observed an excessive production of adrenin in excited animals—his emotion theory. The adrenin forming part of the hemoglobin, and which has been found in the red corpuscles by Justus, is the real measure of the asset of adrenin in the blood, and not what the adrenal bodies secrete, which may be *nil* under normal conditions and excessive under excitement or stimulation.

What connection can this function, this direct connection between the adrenals and the respiratory process, both in the lungs and tissue cells, have with the cure of disease?

By the term "pharmaco-endocrinology" I mean *knowledge of the manner in which drugs influenced the functional activity of the ductless glands.* If, for instance, we can with any drug enhance that of the adrenals, we are able, therefore, to increase at will not only respiratory, activity, but also tissue metabolism, the very foundation of all functions. Again, many investigators, beginning with Abelous and Langlois, have also attributed, on good grounds, an antitoxic function to these organs. A. Marie, in 1912, showed that adrenalin caused active neutralization of bacterial toxins. This important defensive rôle finds its explanation in the function just described, that of sustaining as far as the oxygen supply is concerned, general metabolism. As metabolism includes among its effects stimulation of all organs and tissues which produce all defensive agents, both humoral and cellular, any drug capable of increasing the functional activity of the adrenals must enhance our resistance to disease. Have we any such drug?

As far back as 1903[10] I wrote: "Strychnine, of all agents, stands prominently as the most active suprarenal stimulant" for various reasons submitted at the time. In 1907[11] I further developed this view, citing among other data, H. C. Wood, Sr., and Cerna's observation[12] that the injection of strychnine produced an extraordinary increase in the respiratory air-movement, the increase varying from 75 to 300 per cent. Reichert, Kionka, and Mosso had also noted this phenomenon, which occurred as well in morphinized, chloralized, and curarized dogs as in normal animals. Obermeier[13] had also found that the excretion of carbon dioxide was greatly increased. Briefly, I then showed that its action corresponded, as to metabolic exchanges, temperature, blood-pressure, glycosuria, and other typical effects, with those of the adrenal secretion.

Here again, time has sustained me. In an elaborate study of the subject, Stewart and Rogoff[14] found that strychnine caused a marked in-

crease of adrenin from the adrenals in the dog and cat, ten times the original output having been observed in some instances. The increase was not transient, but persisted during the hour and a half the experiment lasted. "Indeed," they state, "with the smaller doses the effect may go on increasing during the whole experiment." . . . "Doses of strychnine well within the therapeutic range and which cause little or no exaggeration of reflex excitability are capable of producing a considerable augmentation in the rate of output."

Need I urge that strychnine and nux vomica are our preferred tonics, as illustrated vividly by their efficiency in the asthenia following influenza? But this is not the only drug which stimulates the adrenals. If it were not for that curse of therapeutics, the drug addict, we would have in very small doses of cocaine, as well illustrated by the muscular power and resistance with which the Peruvian Indian is endowed by chewing the erythroxylon coca plant, a still more powerful "denfensive tonic," if I may so term it. In digitalis and quebracho (aspidosperma) we have partial though powerful excitants of adrenal activity. In caffeine, coffee, and tea we also possess adrenal stimulants, but likewise only when used in moderation. Indeed, it is the intemperate or immoderate use of *any* stimulant that does the harm; even water drunk in excess has killed.

In excessive dosing lies also a misleading and most harmful feature of experimental pharmacology: the habit of giving internists as the physiological action of a drug, studied in animals, what toxic doses produced in them. The "inhibitory" fallacy of the action of therapeutic doses of adrenalin is a product of this error, the phenomenon being due to *excessive* constriction of the arterioles that supply the organs affected and arrest, therefore, of their functions. As Sollmann[15] says in this connection: there is no "good evidence for the theory of Eppinger, Falta, and Ridiger that epinephrin inhibits the internal secretion of the pancreas." This applies also to Ott's inhibitory action upon peristalsis in so far as therapeutic doses in man are concerned.

The foregoing examples show that it is quite possible to increase at will, with several drugs, the activity of the adrenals and therefore their antitoxic functions. Yet, how control the opposite condition, excessive activity of the adrenals?

We know that various disorders, sexual, muscular, and cutaneous, including hirsuties, etc., the symptom complex also of hypernephroma, are traceable to excessive adrenal activity, or hyperadrenia, or to the presence of an excess of adrenal tissue, adrenal rests, etc. This causes in some cases a pseudo-type of high blood-pressure due to excessive constriction of *all* arterioles, and the increased vascular tension behind

them. Many cases of arteriosclerosis are traceable to excessive adrenal activity. How control this harmful process?

This action of the adrenal secretion, as is well known, is exerted upon the unstriated muscles of the arterioles, as demonstrated by two physiologists, Oliver and Schäfer, in 1894. Now, we have in nitrites *precise antagonists* to this function when the adrenals are overactive. Quite unaware of this action, Cushny[16] writes, for instance: "The seat of action of amyl nitrite is the unstriated muscle of the arteries and veins." Sollmann also writes: "The fall of blood-pressure is due entirely to the extensive vasodilatation produced by the direct action of the nitrite on the arterioles. The vasomotor center is not inhibited." Practice proves that these statements are perfectly true. It is in the cases of persistent hyperadrenia with high blood-pressure referred to above, that I have mainly observed what has rightly been termed pseudo-angina pectoris. How rapidly the nitrites and correction of dietetic errors will remove this disorder is well known. Benzyl benzoate, recently introduced by Macht, acts similarly.

We have now seen that we can actually govern with certain drugs the functions of a set of glands which influence not only the very life process itself through oxidation and metabolism, but also—and what is directly connected with our therapeutic aims—our autoprotective functions themselves.

This is not all, however. Other potent resources are at our disposal. One of these is the thyroid gland. I need hardly recall the powerful influence of this organ on metabolism—or rather on the catabolic phase of metabolism—that which causes the thyroid hormone to first break down fats, and then other soft tissues. But there is a function which physiologists and pharmacologists have always studied very imperfectly because it belongs in reality to a domain other than theirs, that of immunology. I mean the *defensive* function of the thyroid, so active at times that it destroys not only bacteria, toxins and toxic wastes, but also the tissues themselves. Among the large number of sufferers from disorders due to the thyroid apparatus observed in the clinical field—the school to which a great physiologist, Pawlow,[18] referred as "an endless series of the most different and unusual combinations of physiological occurrences which never make their appearance in the *normal* course of life"—I have seen the erethitic and overactive thyroid steadily destroying body and mind, but I have also seen it yield permanently after a focus of infection, whether in the stomach, the intestines, the tonsils, etc., has been removed. Even that destroyer of adolescence, which has been sending 30,000 children to our asylums every year, dementia precox, is beginning to succumb to treatment in which the

anti-toxic and bactericidal functions of the thyroparathyroid apparatus were taken into account. In these cases the phosphorized fats of the cerebral cells were yielding with other fats to the catabolic influence of the thyroid hormone, secreted in excess to destroy the pathogenic agent—of intestinal origin in most cases. Have we not in all these cases evidence to the effect that poisons of various kinds may enhance thyroid activity? Why should not appropriate drugs also do it?

Again, who in the practical field does not know that the cretin and other hypothyroid subjects are highly sensitive to infections and that they succumb promptly unless the cause of their vulnerability is recognized and antagonized when they are exposed to an infection?

Referring to the paper read before this Society last year[19] in which I reviewed this whole question, I will merely recall that in 1907[20] I assimilated the defensive role of the thyroparathyroid apparatus to Wright's opsonins, its influence on metabolism causing it also to enhance the production of alexins in the sense given this term by Buchner, *i.e.* defensive proteins. This interpretation has also been sustained. Leopold-Levi and H. de Rothschild,[21] of Paris, for instance, state: "Sajous has attributed among the functions of the thyroid body a rôle to the latter which he assimilates to that of opsonins and autoantitoxins. Miss Fassin, M. Stepanoff, and H. Marbé have confirmed on their side the influence of the thyroid on the blood's asset in alexins and opsonins." The first investigator did her work in the Bacteriological Institute at Liége, Belgum, the two latter at the Pasteur Institute of Paris. Lt.-Colonel McCarrison, of the Indian Medical Service,[22] reviewing my labors and those of several other observers, also wrote: "While making every allowance for errors of observation, these and other findings of a like nature justify the belief that the thyroid gland contributes largely to the body's antitoxic and bactericidal functions."

Notwithstanding all the evidence available, which collectively would suffice to fill a volume, works of pharmacology make no mention of this defensive function of the thyroid; or if they do, it is merely to quote the observation of Reid Hunt, who found that while thyroid extract decreased the susceptibility of mice to acetonitril, it increased that of rats and other animals to the same poison. Now, acetonitril acting by freeing prussic acid, it is a paralyzant and cannot be expected to increase defensive activity. This applies also to various vascular depressants, which as such impair functional activity including our defensive resources.

The thyroid apparatus being undoubtedly endowed with defensive functions, how can these be brought into play by our drugs? Everyone knows that when all else fails, the iodides will often yield results.

How these beneficial effects are produced has never been revealed. Cushny, for instance, says[23]: "Although the iodides have been more largely used in medicine than any of the other salts of the alkalies, their mode of action is still wrapped in obscurity." In referring to iodine, the same pharmacologist writes, however: "The administration of iodine leads to an increase in the iodine of the thyroid gland," and alluding to the symptoms of iodism and others, he adds: "Many other symptoms which have been observed under iodine treatment obviously arise from the excessive activity of the thyroid gland"—thus making it evident that it is through the "body's antitoxic and bactericidal functions" that the iodides produce their curative effects.

But we have more than the iodides. Our older members will doubtless remember that over three decades ago calomel was practically the sheet anchor as initial treatment in infections. And it undoubtedly saved as many lives as the modern highly trained physician exposes when he administers a nitrite—the household sweet spirit of niter—to offset the fever that Nature is evoking to check a disease. In 1907[24] I studied the effects of calomel and in an article containing eighty-one references, urged that in *very small* doses—never over 1/12 grain doses or less—those we used to call "tonic doses," calomel was probably our most powerful defensive agent. I then wrote, as I would now: "The functions of the pancreas, the thyroparathyroid apparatus, and the leucocytogenic organs being correspondingly activated, the quantity of autoantitoxin in the blood is augmented," all of which the more recent observations of Epstein and Pribram[25] and Krohl[26] have only served to confirm in so far as conferring immunity is concerned. This applies to all infections. In the hands of many, long ago, cases of diphtheria treated with calomel gave a mortality as low as antitoxin. Sellden[27] reported 1,400 cases treated by colleagues and himself with cyanide of mercury, the doses averaging 1/160 grain with a mortality of only 4.9 per cent. Another phase of the value of calomel is illustrated by a personal experience aboard a Cunarder returning from Naples in 1910. The ship surgeon came to me for assistance in checking an epidemic of diphtheria in the steerage which, despite the active and prompt use of antitoxin obtained from an excellent source, caused many deaths. The children, of Hungarian immigrant parentage, being found puny and ill-nourished, I advised, besides the antitoxin, calomel in doses averaging 1/12 grain every hour three times, then every two hours. The deaths ceased at once. By stimulating the defensive activity of the thyroid, the calomel caused the addition to the blood of antibodies which, added to those supplied by the antitoxin directly, promptly overcame the toxemia. Conversely, all those who have treated many cases of Grave's

disease are familiar with the inhibiting influence of ergotin, arsenic, and other agents on the erethitic and overactive gland.

These examples, to which many could be added, must suffice to illustrate the resources that pharmacology offers when endocrinology is used as foundation to attain our object. The remedies used as examples being familiar ones, it would seem as if I had been treading a well-worn path. Yet, progress lies hidden behind their use as regulators of endocrine activity. As excitants of the ductless glands these well-tried agents can be made to promote the appearance, in the blood and cells, of antibodies as active in aborting disease in its incipiency as vaccines have proven efficient in preventing disease. As depressant of the same organs, other familiar drugs can be made to control exuberant activity sufficient to destroy body and mind, a morbid process typified by hyperthyroidism, and which prevails in several destroyers of mankind.

Last year, Sir Almroth E. Wright[28] wrote that the Great War had taught the surgeon that if he excised all devitalized and heavily infected tissues and brought the walls of the wound together, the protective mechanism of the body could, without antiseptics, deal successfully with every kind of infection. What I would submit in the present connection is that we have in the ductless glands intermediaries through which our drugs can, as do vaccines, so enhance the efficiency of that protective mechanism as to arrest disease, before it has had time to compromise life. Organotherapy has enabled us fully to realize the influence of the endocrine upon morbid processes, and pharmacoendocrine therapy will be the second step which will reveal their true importance as weapons in our warfare against disease.

Viewed in this light, pharmacology will assume its true rôle; it must, indeed, eventually become the queen bee of the hive, which all branches of medical science will feed and raise to the highest degree of efficiency. When all this will have been adequately developed and duly apprehended, there will be no more question of abandoning therapeutics in our medical schools, for after all, it is our mission as physicians to cure disease, and to abandon sufferers to its destructive inroads is no less a crime than it is for the soldier to desert the flag in the presence of the enemy.

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# 22nd ANNUAL MEETING

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# CONSTITUTION AND THE PERSPECTIVES OF PATHOGENESIS OF TODAY.*

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The time is ripe for an historiographic research of the ideas and conceptions which leading thinkers in medicine have held concerning the nature of the bodily constitution.

In the study of the causes of disease, we have become absorbed in the wealth of modern investigation and literature concerning mainly two great disease producers. *First, invading microorganisms* and other living infectious agents, and *secondly, chemical substances* arising within the body or entering the body from without. As a third group of causes, we have become familiar with the excitatory or inhibitory influences exerted by an unphysiological nervous system. I do not say pathological nervous system for this expression would range the third group into one or other of the first and second groups, for a decidedly pathological nervous system is either the consequence of an infection or of the deleterious influence of some chemical substance of an exogenous or endogenous origin: but when I say unphysiological, I mean a state in which the central and peripheral nervous system is capable of functioning normally but at times functions in a manner which, while it is not pathological, yet it is not in perfect coordination with the normal performances of the other organs. There is an erethism of the central nervous organs which, while not physiological, cannot be classified as pathological. And yet, this erethism may lead to abnormal states in other organs.

Disregarding the diseases which are admittedly inherited, these three pathogenetic ideas dominate all of our thinking concerning the nature of disease. In this comprehensive view of causes, the medical mind has, however, not given due consideration to another factor in disease production which overtowers in colossal importance all these three causes together; and this factor is the *human constitution itself* upon which the pathogenetic factors just mentioned exert their various influences.

It might be argued that in the very brief scheme of diseases mentioned I have not referred to abnormalities caused by trauma; for example, diseases caused by pressure or violent and mechanical changes

*President's address.

of position; seasickness; aviator's vertigo. But this leads to a great many other diseases which are not due to infection nor chemical causes; for instance, the diseases due to hyperthermia or extremes of temperature in general; exposure to great heat and cold; the effect of radiating energy as a disease-producing cause—sunlight, Roentgen rays, radium emanations, etc.; the effect of electricity as a cause of morbidity; of atmospheric pressure and atmospheric humidity. All of these disease factors in their finality will express themselves in chemical or physical changes, or in injury to the nervous system, secondary to such changes, and thereby come under the brief classification before mentioned.

*Constitution and Disposition.*—Inasmuch as these two terms are frequently confused, sometimes mistaken for synonyms, and even erroneously defined, it will be necessary to give a precise meaning of the terms before proceeding.

These two terms are erroneously defined in the "National Dictionary of Medicine," by John S. Billings and collaborators. They are erroneously defined in part, in the last edition of Webster's Dictionary. In "Hallische Universitätsreden" for 1916, the eminent clinician, E. Adolph Schmidt, states that "constitution" and "disposition" mean the same thing.

*Definition of Constitution.*—The degree in which the organism is capable of overcoming difficulties; of enduring deprivation; the greater or lesser resistance against exogenous injurious influences; the ability to compensate and equalize detriments that have already been caused by mild disease-producing factors.

*Definition of Disposition.*—Receptivity to disease; inherent sensitiveness to pathogenic factors; facilitation for reaction to injurious influences.

Disposition is a quality; constitution is a quantity.

In human pathology, the two conceptions are in reality antagonistic. A strong constitution, meaning increased resistance, is as a rule coexistent with decreased disposition; and a weak constitution, meaning lessened resistance, is coexistent with increased disposition.

Constitution is a variable disease factor, and, according to Martius, is the measure of the resistance of the organism toward pathogenic influences and is composed of the changeable state of individual organs of the body, and therefore constitution varies individually and is different according to different conditions of the organs. The general or total constitution is thereby separated into a sum of partial constitutions. We can therefore conceive of constitution quantitatively, but disposition should be considered only qualitatively. Only those fac-

tors go to make up the constitution which come to the organism during interauterine life.

It is certain that human individuals of different classes and animals of different species are attacked by certain pathogenic factors with greater or less facility, while others of the same class of individuals remain free under the same external and internal conditions. Those that are attacked are designated as "disposed"; those that remain free are called "immune." Classes and species may be equally disposed or sensitive to a certain bacterial poison, but of these, we sometimes find one sensitive to another poison, while the other is immune to the second poison. For example, horses and heifers are equally sensitive to tetanus poison; but for diphtheria, heifers show no disposition, but horses, a very marked disposition; human beings are sensitive to the toxins of scarlet fever and measles, but animals show no disposition to these infections.

We have proceeded far enough to illustrate that constitution and disposition are two entirely different things. For further information concerning these factors see P. Bourcy, "Prédisposition et immunité," in Bouchard's Traité de pathologie générale, T. I. Paris, 1895. From this instructive work one can learn that a series of factors influence and accompany both the constitution and disposition. For example, race, age, sex, the momentary general health of the individual, but, above all, a long series of external conditions which have not yet been exactly defined because they cannot be ascertained in the human being and can only be controlled in disease produced experimentally. To illustrate this point, and also to emphasize the traditional idea of the causation of a human disease, let us summon before our mind's eye the development of a pneumonia. There are three factors necessary in its pathogenesis: (1) A peculiar quality of the body, the constitution; (2) a specific living microorganism, pneumococcus; (3) a sum of contemporaneous external and internal conditions.

Hitherto the medical mind has been tyrannized by an inverted perspective of disease pathogenesis; it has conceived the infecting microorganisms or the toxin, or the physical force as the exclusive factor in the production. This is a total disregard of the immense importance of the human constitution in its innumerable varieties and of the human disposition. This inverted view has been due to an overestimation of the importance of bacteriologic factors, and in its final analysis, is due to the greater facility and control which laboratory methods of culture and staining and experimental infection with microorganisms offer to the bacteriologist. The more important and far-reaching factor—the human constitution—has either been disregarded or it has been taken for granted that it was completely understood. As a matter of fact,

this very human constitution and disposition, which are spoken of in the writings of Aristotle and Hippocrates, and all medical writers since then, are just beginning to be understood in their basic component elements within the last ten or fifteen years. The reasons for the imperfect comprehension of constitution and disposition are to be sought in the almost insuperable difficulties which they oppose to investigation; for not only must the clinical scholar familiarize himself with the details of biochemistry, the effect of physical forces, the relation of the specific personal anatomy of human beings, but he cannot avoid the study of the specific psychology of the human subject that he is dealing with in each special instance.

If, therefore, I recommend a method of observation for the nature of disease which bases it on at least three factors, it is because this mathematical perspective is valuable as a basis for philosophical clinicians in their struggle against the one-sided, rigid method of clinical thinking which has become a form of monopoly of medicine of to-day.

The laboratory worker, like a chemical experimenter, can form his own conditions, lay down and preserve by weight and measure all of the chemical, bacteriological and other factors that enter into his investigation; in short, mathematical circumscription can be made to control his research. But in such complex relations as the natural development of a disease the application of mathematical principles is not feasible and, therefore, it is absurd to speak of the disease as due to a single cause and its effects. In place of this it would be more promising for precision in clinical medicine if any pathological happening or event were deduced from the coaction of a sum of various etiological factors. This is the view which Martius advocates in "Pathogenese innerer Krankheiten," 1909 and which has received the approval of Verworn and Hansemann.

We can make a beginning by singling out from the many more or less important conditions necessary to produce a disease two basic factors: First, the cause; and second, the releasing moment. By *cause*, in our new method of thinking, we must understand the constitution and disposition of the human being in whose body the potential energy of the disease phenomena and the curative processes will play their rôles; it is the endogenous factor. But the *releasing moment* or factor is the microorganism, toxin, or physical force, as the case may be, and which is specific in each disease.

It will be immediately recognized that this manner of thinking is exactly the reverse of what we have been accustomed to up to the present time. "Pathological conditions and processes," said Virchow, "are physiological processes under difficult circumstances," and just

as two normal human beings are never perfectly alike, much less can two cases of the same disease be perfectly alike. There are very few releasing factors, or exogenous causes, as you could call them, which produce exactly the same consequences in all human beings. Perhaps the mechanical trauma and extremes of temperatures may provoke the variable resistance of different individuals in a closely similar manner. But we soon discover with other physical causes (electricity, atmospheric pressure, radioactive substances, etc.) that the individual variation has to be reckoned with more and more.

We must not overlook that in infections it is the effect of toxins that we are dealing with more than the mechanical damage of the tissues by microbes. There are human beings who are so sensitive to definite toxins that they react to the most infinitesimal doses with the severest symptoms, while the majorty of human beings do not react to the same toxins in any measurable degree. The medical systems of the older times called this "idiosyncrasy" and attributed it to a peculiar compositon of the juices of the individual. More modern medicine speaks of this hypersusceptibility as "anaphylaxis" and "allergy."

The disengaging or releasing factors not of microbic origin and which are still frequently used and not understood are such words as *"catching cold," overexertion, exhaustion, disturbance of nutrition.* They seem to be common household words in medicine and yet not understood. Only in the last year have explanations of the process of catching cold been brought forward. It is asserted by H. Schade (Untersuchungen in der Erkältungsfrage, etc. *Münchener med. Woch.*, lxvii.) that catching cold is not an infection nor a neurosis, but an increase in the density of the tissues caused by the cold and a reduction of their elasticity. This can be measured by an instrument—the elastometer. The colloids of the tissues appear to be undergoing a precipitation which is not demonstrable histologically. The effect of cold can express itself in a cold-neurosis; for instance, of the kidney, bladder, digestive tract. The disposition to catch cold has arisen from hyperdomestication, especially from neglect of usuage of the vasomotors of the skin. Especially disposed are the persons with a high degree of moisture in the skin—a general increased water percentage of the tissues; in short, the ancient lymphatic and erethic constitution. It is plainly evident that we are beginning to understand what catching cold means.

The physical changes of the tissues in catching cold are reversible, but if the intensity of the cold is very great, the "colloidity" of the injured tissues remains permanent. Such conditions have been called "cold-gelosis," because normally the almost liquid lymph of the tissues

assumes a consistency like that of gelatine in the injured area. Schade believes that such "colloidity" may occur in muscles, joints, ligaments, nerves, even in the mucous membranes; in one case described by Freitag the cold-gelosis was observable in the cornea in the form of a clouded, opaque area. This condition was reversible and disappeared when warmth was applied.

A similar article by S. Colm—"Leitsätze einer Säftelehre"—explains the movements of the caryolymph by reciprocal physical and chemical reaction between certain colloids of the cell and certain molecules of alkali: the colloids he speaks of as existing in the intracellular substance are albumin and lecithin; the protoplasm is mainly composed of albuminous substance. The lecithin enters the construction of the cell membrane. The functions of life are attached to these two substances together with certain potassium and sodium salts. He describes a current of intracellular lymph caused by the tendency of the unsaturated colloid and the alkali molecules to add related molecules to their substance. According as the normal colloidal content or the alkaline salt content of the tissues varies from that percentage which is normal to the tissues, the function will begin to suffer, although the structure of the cell may continue to appear normal. If the alkaline salts alone deviate from the normal, we have only a functional derangement; but if the colloidal content of the tissues varies, changes in anatomic structure result—we have a pathological tissue. Accordingly, we are introduced to a conception of disease production on a physical basis, as follows: (1) Anatomical or colloid diseases; (2) functional or alkali deviation diseases. This affinity between the colloids, albumin and lecithin on the one hand, and the alkalies of potassium and sodium on the other hand, is made the basis for a new idea of tissue pathlogy which might make the study of the human constitution approachable on a physical basis. We know that the conductivity of any living tissue for the electric current depends upon the presence in that tissue of soluble electrolytes, this being the name assigned to the dissociated ions of salts, acids, and bases. An ion is an element set free by electrolytic dissociation. Therefore, the degree of electric resistance which a tissue normally opposes to the passage of a current is an index of the amount of ions dissociated in the water which bathes the cell protoplasm. In making this test of the resistance of tissues a great deal of preliminary work has still to be done, because the different tissues differ with regard to the degree of resistance which they offer to the electric current and they differ according to their state of rest or work. One of the first facts with which to become familiar in this study is that the greatest and highest resistance is

offered by a healthy tissue and that when a tissue loses its normal resistance it has become diseased.

In recent papers found in the *Journal of General Physiology,* W. J. V. Osterhout of Harvard University has made this type of study of the mechanism of injury and recovery of the cell a special research which he carries out on one of the common kelps of the Atlantic Coast —the laminaria (See also *Science,* April 15, 1921, p. 352).

Osterhout states that the electrical resistance of the living tissue is about ten times as great during life as it is after death, and he attributes this resistance to a layer of protoplasm surrounding the vacuole, a layer so extremely thin as to be comparable to what is commonly called the plasma-membrane.

As the passage of an electric current occurs by means of dissolved ions in this thin layer of protoplasm around the cell substance, Osterhout concludes that the electrical resistance may be regarded as a measure of the permeability of the protoplasm to ions. The tissues have a rather constanct electrical resistance. This normal electrical resistance has to be determined by proper instruments and constitutes the basis for further calculations. If an injury occurs and the resistance falls, let us say 10 per cent., we may say that the injury amounts to 10 per cent.

In the case of laminaria, if the injury caused by placing the kelp in a solution of sodium chloride amounts to 5 per cent., the tissue will recover its normal resistance if it is replaced in sea water. If, however, the injury amounts to 25 per cent., the recovery is incomplete; instead of rising to normal, it recovers to only 90 per cent. of the normal. The greater the injury, the less complete the recovery. When injury amounts to 90 per cent. no recovery is possible in this plant.

Two aspects of injury are described. One is the temporary loss or resistance, which disappears, wholly or in part, when the tissue is placed under normal conditions; this may be called temporary injury. The other is the permanent loss of a part of the resistance which is observed after more prolonged exposure: this may be called permanent injury.

The aim of these investigations has been to apply to the study of living matter methods which have been useful in physics and chemistry. Such fundamental conceptions as vitality, recovery, and death may be investigated by quantitative methods and the investigation of fundamental processes shows that they obey the laws of chemical dynamics. It is too early to apply the results of such studies to an interpretation of such a complex physical and chemical system as the human constitution. And yet I cannot resist the belief that an ultimate understanding of the constitution of the human being will have to be based upon a

knowledge of the physical and chemical processes that are continually going on in the body, and that psychological clinical and philosophical inferences which appear to be not based on biochemical studies had best be held in reserve. It is quite possible to test the resistance of almost all of the tissues of the human body to the electric current; what we lack at present are practical instruments capable of direct applications to the human tissues under various conditions, instruments sufficiently delicate, yet accurate, under the clinical conditions in which their service is needed. Electrical resistance may instruct us as to the amount of dissolved salts in the tissue juices; as to the amount of alkali; and the equilibrium between acids and bases. There certainly will be in the near future an electrolytic method of informing the clinician of the depletion of the body in carbonates and other alkali-yielding substances, for the depletion in these substances constitutes the underlying feature of the tests for acidosis, namely the change in the carbon-dioxide content: (1) Of the alveolar air; (2) of the blood; (3) the concentration of the blood in alkalies, in hydrogen and hydroxyl ions; (4) the tolerance to fixed bases; (5) the alkalinity of the blood so far as it can be determined by titration. In fact, there are such methods in existence already, but they are always associated directly or indirectly with colorimetrics in which the clinican cannot depend upon an instrument, but must depend upon the accuracy of his color vision.

Acidosis is essentially an improvement of the body in alkalies; this being so, it should be measurable by determining the electrolytic conductivity of the various juices that can be obtained from the living human body.

Human constitution is not based only upon the purely and exclusively chemical interchanges, or upon the purely physical changes that go on in the tissues and organs, but depends largely upon the rate of metabolism. Different men and women under normal conditions have different rates of basal metabolism. Dr. Walter M. Boothby (*Jour. A. M. A.*, January 8, 1921, p. 86) states that the normal standard of the basal metabolic rate is not exact; this is due to the fact that all the technical factors necessary to obtain a normal standard have hitherto been observed only in the studies of Atwater and Benedict, Graham Lusk, and DuBois. In fact they are not feasible as yet in the practical pursuits of the clinician. But that there must be fine differences in the basal metabolism of individuals there can be no doubt, and as Dr. G. W. McCaskey states that the Benedict apparatus is of sufficient accuracy for clinical purposes, and Dr. Henry M. Thien states the same for the Jones apparatus, there should be no difficulty in determining

the normal metabolic rate in a large number of healthy human beings under the strict conditions of clinical and experimental control.

For all studies of human constitution the heat phenomena inherent in the living tissues must be made expressible mathematically.

As heat production and basal metabolism are due to the processes of oxidation in the tissues, we are brought face to face with the chemical agents that intermediate oxidation and reduction in the cell, and we are at this date, thanks to the studies of Wieland, Bach, and Frederick G. Hopkins of Cambridge, England, so far advanced that we are made acquainted with the precise agent by which the cell can affect oxidation and reduction. In the Christian A. Herter lectures at the Johns Hopkins University, April 12-14, this year, Frederick G. Hopkins presented his views concerning the oxidation and reduction mechanism of living tissues. The agent which produces these chemical transformations is a substance in which glutamic acid is linked up with cystine. The amido group of glutamic acid is linked up with the carboxyl group of cystine.

Glutamic Acid

Cystine $CH_2S\ CHNH_2\ COOH$

By means of this chemical substance the cell can effect both oxidation and reduction and it denotes a very great advance in biochemistry to have lived in an age where such a great revelation of the workings of the living substance has been made.

Hitherto I have considered the study of constitution only from the standpoint of biochemistry, and this leads to a study of constitution on the basis of the functional achievement of the body. There is, however, another manner in which to study this subject, namely, the anatomical method. This has for its object exact measurements of the size, volume, and contents of the organs. These measurements will give the mathematical expression for the various anatomical apparatuses which are the physical substratum for the work which the body does.

*Anatomical Investigations of the Constitution.*—Exact measurements of the human body in toto and in its parts were first made by the Belgian astronomer and anthropologist Quetelet, but W. Pfitzner ("die Proportionen des erwachsenen Menschen," *Zeitschr. f. Morphologie u. Anthropologie,* ii., 222) proposed certain basal figures for the various measurements, and in our own country, Winfield Scott Hall, in the *J. A. M. A.,* December 21, 1901, proposed a mathematical formula to

determine the median value of human dimensions. I have personally taken up this subject in an article entitled "Anthropometric Studies of the Osseous Proportions of the Human Body, With a View to Obtaining a Mathematic Expression for Enteroptosis" (*Internat. Beiträge z. Pathologie u. Therapie der Ernährungsstörungen.* Bd. 2, Heft 3). But it must not be forgotten that the founder of exact measurements of the dimensions of the human body is that greatest of all painters, sculptors, mathematicians, philosophers, and scientists in general—Leonardo da Vinci. ("Il Canone di Leonardo sulle Proporzioni del Corpo Umano"; Favoro Giuseppe, Atti del R. Istituto veneto di scienze, lettere ed arti, Venezia, 1917-1918, lxxvii., 2, p. 227.) See also J. C. Hemmeter, *Leonardo da Vinci as a Scientist,* in Annals of Med. History, Vol. III, No. 1, 1921.

Beneke later gave exact measurements of volume and capacity of organs of 600 cadavers thereby making a very valuable contribution of the anatomical apparatuses which cooperate to make up human constitution.

Stiller restricted his measurements to special anatomical deviation of a limited number of organs. He thought he had found debility of muscles and nerves associated with a low position of the abdominal viscera and a tenth rib that was not attached to the costal arch, and he constructed from this a peculiar disease which he terms "morbus asthenicus." It was a broadening out of the views which Glénard had already announced concerning splanchnoptosis. However meritorious the studies of Stiller may be, and they constitute a brilliant clinical advance of the state known as enteroptosis, nevertheless it must be evident that organ abnormalities do not constitute a disease until the displaced organs function irregularly. What Stiller described was not a constitution, but a disposition; it was not a disease, but rather one of the factors that predispose to a disease if certain other exogenous factors are added.

The whole subject has been gone over again by myself in an article published in the *Interstate Med. Jour.,* xix., 3, 1912. ("Splanchnoptosis, or Constitutional Neurocardiovascular Asthenia with Osseous Dystrophies and Disproportions—Enteroptosis.")

Among the anatomical deviations that may contribute to form characteristic constitutions are abnormal connective tissue developments, the thickness of the wall and the width of the aorta; endemic goiter; and the so-called status thymicolympthaticus. All of these conditions are found only as narrowly circumscribed or restricted organ abnormalities and they are not in themselves sufficient to make up a constitution. Above all things, it is necessary to insist on a definition of what a constitution is in a normal creature. (See definition previously given.) The

great problem of research concerning the human constitution must be to define at least part of its entity in mathematical terms.

In all measurements of the type quoted in the preceding, we can deal only with the supporting tissues and structures—the bones and connecting tissues, and it must be evident that from such canons of human proportions, we can obtain only mechanical conceptions concerning the totality of the human machinery. When we get to other tissues, for instance, the central nervous organs, and the glandular organs, we become convinced that it is not structure and form, but the achievement and the work done by the organs which is of greatest importance in the question of constitution.

*Functional Investigations of the Constitution.*—Every expression of life of the organism is bound to its basic elements, the cells; but deviation of function, either depressed or exalted, can occur without any demonstrable change in the anatomic structure of the cells, and for the practical clinician function is more important than structure, for as all endeavors of therapy must be directed toward the restoration and maintenance of function, it is essential to know what a diseased lung, liver or spinal cord may still be able to accomplish rather than to ascertain how these organs appear under the microscope. This has led to the great development of functional tests which have revealed the fact that conditions of insufficiency of the kidneys, the heart, the liver, and so on, may exist without any morbid state becoming manifest. Such latent or potential organ insufficiencies are discovered in the entire absence of symptoms, and they constitute partial factors of constitution.

The clinical investigator on discovering such secret defects in an apparently healthy body, naturally becomes elated over the penetrating power of instrumental and chemical research, a state of elation that rapidly calms down when he asks himself the question—"What is the cause of these potential organ insufficiencies?"—for certainly we have the secret of the constitution not plainly before us by merely establishing a latent or potential organ insufficiency—we must still find out what produced this.

In an address to the American Therapeutic Society in Washington by invitation of the Program Committee of 1913 on "Hypertonicity and Hypotonicity of the Vagus and Sympathetic Nervous System" I called attention to certain neurochemical synergisms of the normal body and the pharmacodynamics of certain exogenous and endogenous chemical substance. The address was published in the *N. Y. Med. Jour.*, January 17, 1914. A part of the article deals with the question whether or not disturbances of the endocrine system can be recognized before they have led to distinct disturbances in the organisms. At that date the investigations of Eppinger and Hess, and of H. H. Meyer, concerning

the provocative introduction of adrenalin and certain pharmacal substances had already been undertaken, and they revealed a definite reactability, that is, a readiness to respond to these chemical substances in certain systems of nerves, especially the autonomic and sympathetic systems.

The entire inspiration to this field of research is due to Brown-Sequard, and the coordination of countless physiological discoveries and anatomical research with the objective facts elicited from clinical investigation has been illuminated by no one in such talented manner as by our fellow member, Sajous. One has only to read and study his chapters on the Internal Secretions in Their Relations to Pharmacodynamics to be impressed with the truth that here is a new revelation of therapeutics, not new in the sense that nobody ever announced such ideas before him, but new in the clinical sense that at last the dawn of a new therapy has broken, a therapy that is at once rational and practical.

The labor of this brilliant coordination of the facts of science with the demands of practice could only have been accomplished by an encyclopedic mind. But also concerning the nature of human constitution, the study of the endocrine system throws a brilliant light. It is established that the anemia of young females at a certain age is not as Virchow thought, due to congenital narrowness of the aorta, but to defective function of certain blastogenic glands and of the bone marrow. There is an endogenous obesity which is independent of the amount of food taken in. This obesity can continue even when the food is reduced below the caloric requirements; for it is due to certain disturbances of the thyroid gland and the pituitary body. We know that diabetes is associated with the internal secretion of the pancreas.

There are revolutionizing dystrophies of the entire human frame which change, as it were, the tribal appearance of the human being—mongoloidism, eunuchoidism, infantilism—which are due to a disturbance in a reciprocal balancing of various endocrine systems and the status thymolymphaticus is only intelligible if it is viewed in the perspective of disturbed internal secretion working on the total organism.

That vast field of research on immunity which has been blasted out of the unknown by Metchnikoff and Ehrlich, which is based upon the explanation of the formation of antibodies, etc., as well as the defensive ferments of Abderhalden, are human endeavors aiming not only at the cure and prevention of disease, but unconsciously laying bare some of the secrets of human constitution; for antibodies and defensive ferments are products of body cells.

When we ascertain by analysis of blood that certain specific im-

mune bodies are circulating in the body we gain a profound insight into the economy of the organism and, to some extent, into its disturbances. But the entire constitution and the entity of the disease afflicting it is even then not open to our eyes; for most of the factors that go to make up the human constitution are not acquired by the individual during life, but the greatest part of these factors is inherited. The factors inheritance, as well as of acquired constitution, lead us to a brief consideration of heredity.

*Constitutional Immunity Due to Selective Adaptation Between the Human Being and the Infecting Organism.*—Prof. Max Neuburger, in his historic studies of the epidemics of antiquity, has emphasized the impossibility of ascertaining in our time what the exact diagnosis of those diseases may have been. In very remote periods, for instance, in the plagues described in the Old Testament, (II. Samuel, xxiv., 15, 16; I. Chronicles, xxi., 14-16; in this epidemic 70,000 people lost their lives; Numbers, xvi, 49, the epidemic of Korah, in which 14,700 people died) a diagnosis in our sense of the word was not attempted, in fact, was impossible. Such a master of historiography as Thucydides has described a destructive infectious disease which invaded Athens during the Peloponnesian war and given a minute and detailed account of the epidemic; and yet no clinician of the present day is able to state what disease this was, and Iwan Bloch maintained that the venereal plagues mentioned in the Bible (Baal, Peor) are not the same as present-day lues, etc.

The truth is that in the course of thousands of years reaction between the cause, by which I mean the peculiar constitution and disposition, and the releasing factor, the microorganism, may change so fundamentally that their outward phenomenon called the disease is no longer recognizable by the posterity two or more thousand years remote and does not fit into any of their classifications. There may have been many diseases in prehistoric times of which we have no record whatever, and there hay have been others which thousands of years ago presented pathogenetic manifestations which to-day cannot be forced into schemes of clinical classification.

But there is still another factor in the ceaseless adaptation between the human constitution and pathogenetic factors, and this I have called the reciprocal selective adaptation between the human constitution and certain infective organisms.

It is well known that the bacteria of different types lose their virulence and power to form toxins readily. It is also known that these two properties can be increased when a certain strain of bacteria undergoes what is known as animal passage, that is, the microorganism is made to exist for a time in the bodies of one or other of the mammalia.

In artificial culture microorganisms rapidly lose their virulence. It is also known that the virulence against one species of animal is as a rule specific and that virulence specific against one type of animal may go hand in hand with diminution of virulence against another type. Martius, in his "Pathogenese innerer Krankheiten" (1909), gives the evidence that pathogenicity is not a constant property characteristic of bacteria, as for instance, proteolysis is characteristic of certain enzymes, like pepsin or trypsin, but rather that pathogenicity signifies the ability of the bacteria to react in a specific manner when they come into a medium corresponding to their biologic requirements. Now this is nothing but a functional adaptation to certain chemical and physical conditions which the life of the bacteria require. The bacteria, in fact, have their constitutions and dispositions also, just like human beings.

In the following I will endeavor to make clear that infectious diseases that may have existed during former historic periods of the human race may have disappeared entirely, because the reciprocal relation between the constitution of the human and the constitution of the bacteria have been so adapted reciprocally that instead of a disease a form of symbiosis (living together innocuously) has been established.

Let us take the instance of one single infective organism—the bacillus of typhoid fever. It is well known that this organism, when existing in nature, loses its power of multiplication, eventually dies and disappears; on the other hand, by continued animal passage, or change of the host in which it then forms what the clinician calls an infection, its power of multiplication can be indefinitely increased.

Now it happens that the temperature and the chemical composition of the human body coincide with the conditions of the most prolific growth and most intense effectiveness of all the vital functions of these bacteria. In other words, the human body presents the optimum physical and chemical conditions for the growth of the typhoid bacilli, and but for the human body this bacillus and a large number of other pathogenic bacteria would be doomed to extinction. In comparing the colon bacillus with the typhoid bacillus, it is found that the *Bacillus coli* can live without human body, and by many bacteriologists is considered ubiquitous.

The next step in the development of the symbiosis is the phenomenon of the so-called human bacillus carriers. It is known that human beings can carry pathogenetic germs in their bodies for many years without being sick themselves. There are two classes of carriers: (1) Those who have already gone through the specific chain of pathological events, called in this case typhoid fever; and (2) those who have

never had typhoid fever and yet show typhoid bacilli in their stools. In both instances the bacilli live in the optimum condition.

Dr. L. Radcliffe Grote of Halle does not consider that this carrying of bacilli is an accidental collateral phenomenon of the disease caused by fortuitous immunity processes in specific individuals; but he conceives it as the end result of a long series of processes culminating in a reciprocal adaptation between the infecting organisms and the host. Both factors have eventually reached a form of coexistence which corresponds to the biological conception of symbiosis.

The conception of symbiosis demands that the coexistence of two different kinds of organisms shall result to the advantage of both. The bacilli of the coli group offer to the human being a very distinct and important advantage because the glands of the digestive tract secrete no ferment which can digest cellulose. The splitting up of the capsules of most leguminous vegetables can be accomplished only by the intestinal bacteria, and in the experiments of Schottelius it was found that hens and goats which were kept under absolutely aseptic and sterile conditions of life did not grow as well as animals of the same strain who were permitted to fill their intestinal tract with bacteria.

Not all human beings are fitted to develop a state of symbiosis with certain bacteria, and not all bacteria have the properties fitting them to mutual adaptation with the human host. Specific and peculiar constitutions in both the host and the microorganism are necessary.

This process of mutual adaptation no doubt is one of the phenomena of natural selection and may have been going on between our race and parasitic infective agents for millenniums. Diseases which may have once wiped out human beings by the hundred thousands to-day do no longer exists (Psalm xc., 3) and infectious diseases of a severe type to-day may be unknown to the clinical historiographer of the year 3000. "*A disease, accordingly, is a phenomenon of collision between the biologic requirements of an infective organism and the human constitution organism in their effort to reach symbiosis.*" The vital necessity of both organisms conflicts in this struggle and the disease process is the expression of a process of adaptation between the host and the parasite. (L. R. Grote, *Münch. med.* Woch., 1920, 38.) According to a footnote in this article Prof. von Drigalski made the observation in epidemiological investigation before 1904 that the typhoid bacillus can displace the colon bacillus completely and fill its biologic rôle in our body. He studied persons who permanently excreted pure cultures of the typhoid bacillus in their stools. These observations cannot be interpreted in any other way than that the typhoid bacillus has assumed the total work of the intestinal flora in man, and this means a most

extensive adaptation of the typhoid bacillus to the requisites of the human intestine. Thus in this intensely interesting form of adaptation and natural selection both the human host, as well as the bacteria, undergo very grave fundamental transformation. The evident antagonism between both organisms during the disease has to be transformed into a reciprocal adaptation requisite to symbiosis. For both factors, host and parasite, the destructive element of the disease represents a very dangerous stage of transition. The human organism meets and equalizes the exigencies of this dangerous transition by the requirement of immunity. The bacteria meet them by colossal celerity and power of multiplication. Some bacteria develop so-called resisting permanent or enduring types.

I have gone into this phenomenon of symbiosis between host and parasite because it is not considered as one of the elements of the human constitution, and still it must be evident that it is a process which is continually going on almost unconscious to the clinical observer.

*Heredity.*—The properties or peculiarities which an adult organism capable of progeny possesses may be divided into three groups, according to their derivation: (1) The great majority of all properties of an organism were already possessed by his ancestors; these are the inherited properties. (2) There are properties by which an organism, it is true, differs from its ancestors and therefore are not inherited; yet he possesses them from the date of his birth onward; these are the congenital properties. (3) Every organism shows properties which he does not acquire until after his birth during the course of his individual life; these are the acquired properties.

The hereditary and congenital properties are conditioned by peculiarities of the blastogenic cells. They are therefore termed *blastogenic*. The acquired properties at the present time are considered as independent of the germ-plasm. They are pure acquisitions of the *soma* and, therefore, defined and distinguished as *somatogenic* properties.

If the differences between descendants and ancestors are very slight, and if, in addition, the differences between various individuals of the same brood among themselves and with the parents are connected by transitions, so that they can be brought in a continuous series, then we speak of *fluctuations* or *continuous variability;* but when these differences between the parents and descendants are very great, and also if the brood can be separated into two sharply distinguishable groups which cannot be arranged in a continuous series, then we speak of *mutations.*

To-day one often meets with the conception that only the mutations are inheritable, and not the fluctuations. This is due to the fact that the

mutations are strikingly different from the original stock and therefore are more easily detected.

Thus far it has not been satisfactorily demonstrated that somatogenic properties are really inherited. The experiments of Standfusz, E. Fischer, Sumner and Kammerer seem to prove the transmission of somatogenic properties, but Tower found that in repeating some of his experiments, that the influence of the experimental changes on the blastogenic cells could not be excluded. Almost all these observers, it was later on proven, had practised an unconscious natural selection, and Jennings concludes that the problem of hereditary transmission of acquired characteristics in the infusoria meets with the same difficulties in the protozoa as in the metazoa.

As heredity plays such an important part in the transmission of human diseases, it must be evident that this subject cannot be considered as finally closed until it can throw light on human pathology, which long experience has demonstrated in certain definite forms to be transmissible.

The modern conceptions concerning the proliferation of the maternal and paternal blastogenic cells explain the process in such a way that the cells that serve future generations early separate from those cells which are to form the rest of the body; in other words, the blastogenic cells slumber in the germ glands until maturity of the individual, and thus the idea of continuity of blastogenic germ plasm brings with it the other idea that the entire body, all organs including the brain and their activities, are merely appendages for the preservation of the blastogenic cells which decide the species.

Degeneration of the body constitution acquired during life may affect the germ plasm, but hardly in a specific form of change of its inherent qualities so that the identical constitutional abnormality acquired by the parents shall be in evidence in the descendant. Such an influence has been termed parallel induction of the somatogenic and blastogenic cells.

In my article (*loc. cit.*) on the anthropometric measurements, with a view to establishing a mathematical expression for enteroptosis, I expressed the opinion that a frequently or continually repeated parallel induction of body and blastogenic cells might affect the chromosomes and plasma of the latter by summation of the stimuli. I mean that eventually a specific change may be produced in the blastogenic cells, although this may not be evident in the first or second generation. A conception like this meets with great difficulties unless an exceedingly intimate chemical connection between the somatogenic and blastogenic cells is conceded. That such a connection exists can be no doubt, for all the gonads, in addition to their external function, have also an internal

function as endocrine glands. This explains the fundamental changes of the entire body during the development of maturity and the peculiar disturbances of the constitution in eunuchoidism and allied states; and conversely there is a dwarfed and defective function of the gonads when the pituitary body is diseased. The functions of the entire organism consists of a complex reciprocal correlation of the organs themselves, and there is possible, also, a functional adaptation of the growing, and yet undifferentiated cells to new external conditions of life.

If this adaptation concerns organs that stand in a close altruistic relation to the blastogenic cells, then it is conceivable that during the course of long periods of time, when these influences are effective in the same manner through generations, new inheritable properties can be acquired. The Darwinian theory of natural selection conditions a far-reaching variability of the blastogenic cells, and if some biologists assert that natural selection is the only way of evolution, then this power of variability in the germ cells must be infinitely great and must have been present already in the very beginning of organized matter. Plate asserts, therefore, in view of the insufficiency of these conceptions, that the principle of the hereditary transmission of acquired characteristics is a logical demand upon the thought of future investigators.

*Overculture and Race Degeneration.*—When the deleterious changes of the constitution are not confined to individuals, but extend to entire races or people, they can only be explained by influences which have worked upon long series of progenitors in the same manner. Such changes are noticeable among our race at present, and to convince the casual reader of this I will merely mention a few that will spring into the attention of anyone who cares to undertake the observation: (1) The increase in the inability of young mothers to nurse their children; (2) the increase in dental caries; (3) the increase in the number of individuals under thirty who have an impaired vision; (4) increase in otosclerosis; (5) the increase of rachitis; (6) the increase in the digestive disturbances and faulty nutrition; (7) the increase in psychic instability (psychasthenia, neurasthenia).

The race is losing part of its aboriginal instincts whereby the adaptation and reaction to environment was entirely automatic and subconscious. The race has become so accustomed to an extensive protection against all dangers to our existence that it has come to an insufficient use of our locomotor apparatus—nerves, muscles and bones. In addition, the modern means of transportation and the intense strain upon the central nervous system, created by the close cohabitation in colossal modern cities, leads to rapid exhaustion of these noble master

organs. All the achievements of culture by the progress of hygiene, artificial immunity, sanitation, physiologic dietetics, operative technique, cannot compensate the race for the colossal loss of automatic subconscious adaptation of our organism to nature, if this should continue.

All these advances that I have mentioned cannot restore this biocosmic reciprocal automatism between man and nature. The aim must be to induce the race to get back to nature; a colossal and almost impossible task when one reflects that it means the dissolution of the big cities; the restoration of human beings to a life in the country, or at least in so much country that each individual is assured the requisite amount of natural earth, air, sunlight and immunity from the contamination of great cities.

*Mendelian Theory of Inheritance.*—In 1865, Johann Gregor Mendel published under the title, "Versuche über Pflanzenhybriden," in the Proceedings of the Society of Natural History of Brünn, Austria, his law of heredity. He made prolonged experiments in crossing varieties of the pea (*Pisum sativum*). His paper was overlooked until attention to his remarkable results was called by DeVries in 1900; he and also Correns and Tschermak at the same time independently rediscovered Mendel's law. Mendel selected seven pairs of characters, such as the shape of the ripe seed, of the cotyledons, of the seed-pod, color of the seed-skin, length of stem, etc. Large numbers of crosses were made between peas differing in respect of one of each of these pairs of characters. It was found says Bateson, that in each case the *offspring of the cross exhibits the character of one of the parents in almost undiminished intensity*, and intermediates which could not be at once referred to one or other of the parental forms were not found. *"In the case of each pair of characters there is thus one which in the first cross prevails to the exclusion of the other."* This prevailing character Mendel called the dominant character, and to the other he gave the name of recessive character.

Every Mendelian element in the germ plasm is represented by one or more inheritance units which are called *factors* or *genes*. Weismann and DeVries assume them to be living particles, and other theoreticians in inheritance assume them to be enzymes. Continued amphimixis of brother and sister in the human race has not occurred, and therefore, in our race, we have hitherto only accidental resemblances to Mendel's law. Marriage among close blood relatives may have been a racial necessity in the very earliest prehistoric state of the human race. The Mendelian idea that a descendant always has a definite calculable part of the heredity mass of his ancestors, but not a molecule of strange germ plasm, is with the human being an impossible conception.

Gaton, on the basis of an investigation of heredity in certain animals, has formulated his results to the effect that, in a given case, 0.5 of the inborn characteristics will be derived from the two parents (0.25 from each), 0.25 from the grandparents collectively (0.0625 from each), 0.125 from the greatgrandparents taken together (0.015625 from each), and so on in similarly diminishing proportion. This law, futher elaborated by Pearson, and in some slight degree corrected on obstruse mathematical grounds, is by him acclaimed as a scientific generalization of immense importance, comparable for its power of resuming in one brief statement innumerable facts, to Newton's famous law of gravitation. Apparently, on this hypothesis, the inborn qualities of an individual will be fully covered by the sum of inherited qualities (S—1) only when the lineage has been carried back *ad infinitum*. Go back only a few, say ten, generations, and you have already reached the source of the great majority—some nine hundred and ninety-eight out of each thousand—of inherited characteristics. (Chas. J. White in *Makers of Men*.) But go back as many generations as you like, and a residue, albeit infinitesimal, of inborn qualities, not yet accounted for, will confront you still. And in dealing with human individuality, it is to be noted that some quite inconspicuous but deep-seated quality, of remote and obscure origin, may quite well be, in any given case, the little leaven that leavens the whole lump. Hence, in part, the apparently paradoxical results often attained by consideration of the recent family history of remarkable personalities. Beyond all available human records, beyond all human ancestry, beyond the prehuman mammalian and submammalian stock, beyond the primeval monocellular starting point, even to the groundwork of inorganic nature, we must pass for our ideal completion of the sum of inborn mental and physical characteristics. There the manifestation of the contemporary human career has its dawn; there the *Ego* begins its æonic march towards the fulness of predestined activity. (White.) It is further to be noted, with reference to Galton's law, that it is a statement of averages only, for "the introduction of the Mendelian law, combined with the results of recent cytology," makes it likely that in any given individual the maternal and paternal factors lie side by side and separate out in the gametes (ova or spermatozoa) of that individual so that we do not inherit equally from all grandparents of each generation, but all from some and nothing from others.

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# HISTORY OF ALCOHOL AS A SUBSTANCE FOR HUMAN CONSUMPTION

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The word "alcohol" comes from two Arabic terms, al, which is the article, corresponding to "the," and *kahal* meaning of finely divided powder.

Originally, alcohol was the term applied to any finely divided body, but later became applied to the spirit of wine, after it had been brought to its greatest purification. Kopp, in his Geschichte d. Chemie, 1847, IV Part, p. 271, narrates that with the Arabians and also Spaniards, the word alcohol means antimonium sulphate—and not the $C^2H^6O$, but that the volatile part of wine was rendered freer from $H^2O$ by placing it in contact with tartrates (Wein Steinsalz) and all salts are called "alcali" —thence was derived the term *spiritus alcalisatus*—which was corrupted into *spiritus alcolisatus*, and this word went over into *alcool spiritus vini*.

The ancients had no intimate knowledge of alcohol as such, although they consumed wine and beer. Their distillation apparatuses were too imperfect. The distillation apparatus was first introduced by the Alexandrians.

In 950 the Arabic physician, Rhazes, described a method of preparing alcohol, but does not mention its combustibility. In 1440 Giovanni Mick-Savonarola published a method of testing brandy for the amount of $C^2H^6O$. In 1784 Lavoisier demonstrated the composition of $C^2H^6O$. In 1784, Carl Wilk Scheele showed that when $C^2H^6O$ and organic acids form ether, this ether can reversely be converted into the acid and $C^2H^6O$ used. In 1796, absolute alcohol was made by Tobias Lowitz with dehydrated (freshly heated) calcium carbonate.

Adherents of alcoholic beverages frequently maintain that the use of alcohol like that of all other stimulants is due to a deep-seated necessity of the human race. Alfred Grotjahn, in the thirteenth volume of the Library of Social Sciences (Bibliothek der Socialwissenschaften), which appeared in 1898, makes the assertion that the desire for alcoholic beverages has for all time been so general with all peoples that the same must be regarded as a common human heritage. Older authors speak in the same strain. Even Pappenheim asserts in his work. "Sanitätspolizei," that alcoholic beverages seem to have been evolved to meet an everpresent requirement of the human race. We can only hope to do away with inebriety and the stronger alcoholic mixtures.

In contravention to this, Baer states in his standard work: "The

human race surely has existed countless ages without using these artificial remedies. Many races exist to-day or have lived recently who developed no feeling of instinctive necessity for these things until they became cognizant of them."

I have made it my business to show that the whole alcoholic question is the product of a very slow process of evolution from a very modest beginning to its present proportions, from a slight inclination to its subsequent abuse.

From prehistoric times to which the historic period compares as a small fraction of time, no clue has come down to us in regard to the use of alcohol. Man could only consume that which nature voluntarily offered him. Very gradually did he develop his customs and his tastes through learning to adapt the forces of nature to his purposes.

As glorious as this victory of consciousness over subconsciousness really was, it brought with it many customs and habits which, being in opposition to the laws of nature, superinduced sickness, misery, and crime. As the prime offender we have the consumption of alcoholic beverages. Their first appearance is enshrouded in mystery. The first mixtures of sweet wines and other fermented beverages with much water had doubtless an agreeable effect, as well as the ensuing mild paralysis, which revealed itself as a heat sensation and a stressing of the emotional propensities of the individual.

Tolstoi maintains that the chief objective of alcohol consumption is the paralysis of the conscience. If these primitive people had been aware that the aforesaid phenomena of paralysis were in fact symptoms of poisoning, and had had some knowledge of the concomitant and after effects of same, they would have been still more cautious than they really were with their discovery. Thousands of years after the first production of wine it was used in small quantities, highly diluted, in conjunction with meals. Among the Israelites, who were the first to produce wine, drunkenness was not known to any extent.

The Israelites preserved their wines in skins and jugs. The German, French, English, Italian, Latin, and Greek words for wine are derived from the Hebrew "yain." Wine was used with meals and for devotional purposes. There was no abuse and hence Moses saw no necessity to formulate regulations in regard to its consumption. The Semitic peoples, more particularly the Phoenicians, introduced wine to all the Mediterranean nations, of which we shall refer especially to Egypt and to Greece. To be sure, the Egyptians had concocted a drink from barley and bitter herbs and the Greeks had done the same through the fermentation of dates, figs, apples, and honey, but wine rapidly supplanted these.

It is necessary to emphasize that such a thing as drinking apart from meals, and also the existence of inns, was out of the question. The Greeks were the first to use wine not as an adjunct to meals, but at entertainments devoted to sensual enjoyment. They consumed wine greatly diluted with water, while listening to the music of the flute and kithara, while nude female slaves danced and sweet smelling odors permeated the halls. Rough, boisterous conduct at these affairs was regarded as beneath contempt, barbaric. There was no drinking in the open or at political gatherings, gymnasiums, or baths.

Greek emigrants introduced the manufacture of wine into Sicily and Italy. Wine rapidly supplanted the fermented brews of barley and honey of the Romans. It thrived everywhere on the peninsula, was diluted with sea-water and consumed at meals. At first drinking by women and young men was discountenanced; but very gradually, near the end of the imperial period, women took up drinking. The feeling was about the same as is now that regarding smoking by women.

When intemperance had become a fact, particularly with the well-to-do classes, the first measure against the use of wine was called into existence by Domitian (87-96 A.D.). Domitian forbade the development of new vineyards and ordered the demolition of one-half of those in existence. This regulation remained in force 200 years. It was annulled by the Emperor Probus (276-282 A.D.).

Rome's historians and moralists do not make any references to alcoholic abuses of the middle and lower strata of society. We can assume, therefore, that in the case of the ancient peoples, there was really no alcoholic question. This first sprung into existence when the Romans came in contact with the barbarians. Just as happens to-day, when a highly civilized people introduces a narcotic to a savage people, the foreign nations, such as the Scythians, Thracians, Macedonians, Gauls, and the Germanic tribes adopted wine with avidity, drinking it unadulterated. Nearly all terms pertaining to the raising and making of wine may be recognized as Latin derivatives.

Although the Teutons like the Egyptians, Greeks, and Romans, had a mildly intoxicating drink, derived from honey and called meeth, it is, nevertheless, very improbable, at any rate not demonstrable, that they produced the same in large quantities, as the art of husbandry was not developed to any extent with them.

With reference to the frequently cited passage in Tacitus' "De More Germanorum" 22, 23, that Teutonic armies suffered defeats owing to widespread drunkenness, let it be said that these occurrences were not, as is frequently assumed, the result of an inherited trait, but a

phenomenon corresponding exactly to the effect of spirituous liquors on American and African indigenous tribes.

Some Teutonic tribes evidently recognized the great danger of the new drink (for which see Cæsar's "De Bello Gallico" Liber 4, Chap. 2), where the Suevi are reported to have instituted measures prohibiting the importation of wine.

After the fall of the empire the barbaric custom of drinking unadulterated wine to the point of intoxication, spread through Europe. Such was the state of affairs during the time of the racial migrations. Christianity might have been an effective check to the growing alcoholism, but unfortunately, several centuries had elapsed since Christ had first offered his doctrines to the world. In His time the drink habit was of such insignificance that there was just as little reason with Him as had been the case with Moses, to agitate against it. With the third religious founder, Mohammed, things were different. In his time the drink habit had reached such proportions that he started the greatest anti-alcohol movement known up to that time, and succeeding in eradicating wine growing in all conquered regions.

A peculiar accident would have it that Mohammedans, that is, Arabian physicians, succeeded in the eighth century in distilling brandy from wine, which discovery was to be devoted to healing purposes. They called the new product *al kohol,* that is, "fine extract." It was a very unfortunate incident, in so far as it encouraged to an enormous extent, the abuse of alcohol. Later on, Occidental alchemists took possession of the newly acquired knowledge. After repeated distillations, that is, rectification, a more concentrated spirituous liquor was obtained until finally Basilius Valentinus, a Benedictine monk, succeeded in producing an almost pure alcohol. The belief spread that this wonderful thing, "spiritus vini," was an all cure remedy for diseases and also a preventive agent against epidemics, such as the pest.

Michael Schrick, in the year 1482, at Ulm, offered this precept in his work, entitled "The Burnt-out Waters," published at said time and place: "Whoever drinks one-half spoonful of burnt wine every morning, will never become sick." The price of this "burnt wine," however, was so high at that time that only the well-to-do classes could carry out the suggestion.

In the meantime, wine culture developed northward up to the limits set by the climate itself, that is Central Germany. In North Germany, after the Teutons had developed their knowledge of agriculture, there was produced an alcoholic stimulant from barley, which was called in Anglo-Saxon "bere." This was also done in northern Gaul.

In the twelfth century, John the First of Flanders and Brabant, known as Jan Primus, became such a patron of the brewer's art at Bruges, that he evolves later into Gambrinus, the legendary patron saint of the brewing industry. In the fifteenth century, the art of brewing made a marked advance when it acquired knowledge of the malting process, succeeding in making a much more palatable and stable beer than was known before, particularly in Einsbeck, Naumburg, Hamburg, and Brunswick.

With growing wealth and consequent luxury, debauchery and intemperance became always worse, so that Emperor Maximilian the First at various diets from 1495 to 1512, took a most decided stand against the drinking habits of the well-to-do classes. About 1600 the first temperance society was founded. The members of this society had to agree not to drink more than fourteen goblets of wine a day.

A new advance in the technique of making spirituous liquors made the latter accessible to the lower social classes. It was the manufacture of brandy directly from corn. This discovery made in the sixteenth century was spread everywhere, into the smallest hamlets, by the soldiers during the Thirty Years' War.

Duke Ernst August, in 1691, expresses his great regret in an edict that spirituous liquors which were really intended for purposes of healing had become an instrument of debauchery, and that even in the places where they could be bought, drinking rooms existed in which such debaucheries were carried on.

The wrong assumption that spirituous liquors gave strength and health was largely responsible for the diffusion of the custom. In Hungary in 1550 miners regularly received apportionments of alcoholic stimulants to increase their efficiency. Soon after this, the beginning of the drink tip, or "trinkgeld," as it is called, makes its appearance, supplanting the bath tip. In the fifteenth century every village in Germany and Austria had its public bathhouse from which was developed later the barber shop. Apprentices and servants received on Saturdays and on the days preceding holidays, the bath tip. In the course of time the opinion became current that pest and syphilis, which had been imported from France, were transmitted in the bath rooms. Spirituous liquors were regarded as preventives of these dread diseases, and thus the drink tip replaced the bath tip.

As the manufacture of spirituous liquors became cheaper and cheaper, the demand for them increased and in consequence the injurious effects became worse. Perhaps it was necessary to have the whole matter reach such enormous dimensions as to make the necessity for calling a halt seem more imperative.

In reply to such writers who care to assert that the drinking habit is really the result of an inherent instinct, I shall refer them to this assertion from Darwin's pen, to the effect that since an acquired habit becomes hereditary, the similarity between an acquired habit and and instinctive trait is so great that the one is not susceptible to differentiation from the other.

To the impartial observer who can follow the development with an unbiased eye, it would appear that this gradually expanded habit was not instinct at all. I believe that all drinking customs to the contrary notwithstanding, the opinion which the great Dutch savant Donders expressed in the year 1853, in his work entitled "Foodstuffs," still holds good, to wit, "If from to-day on not a drop of spirituous liquor is consumed, the instinct will become after a few generations dormant, if not entirely eradicated."

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## THE PHARMACOLOGY OF ALCOHOL AND ITS INFLUENCE ON METABOLISM

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"What wonders does not Wine! It discloses secrets: ratifies and confirms our hopes; thrusts the coward forth to battle; eases the anxious mind of its burden; instructs in arts. Whom has not a cheerful glass made eloquent! Whom not quite free and easy from pinching poverty!" Thus spoke Horace. When we speak of alcohol we are understood to refer particularly to the so-called grain alcohol, $C_2H_5OH$. Yet would we fail in our undertaking if no reference, though passing, were made to other alcohols which are included in the series of this type of hydrocarbon compounds and which, according to Baer, show a toxicity progressing with the n — value of the compound. Thus he finds:

| Alcohol | Formula | Toxicity |
|---|---|---|
| Methyl | $CH_3OH$ | 0.8 |
| Ethyl | $C_2H_5OH$ | 1.0 |
| Propyl | $C_3H_7OH$ | 2.0 |
| Butyl | $C_4H_9OH$ | 3.0 |
| Amyl | $C_5H_{11}OH$ | 4.0 |

Or, taking the later figures of Macht, and of Morgan and Cooper, and Kamm, we find the following:

| Alcohol | Macht Toxicity to Cats | Morgan and Cooper Germicidal Power | Kamm Toxicity to Paramecia | Albumin Coagulating Power |
|---|---|---|---|---|
| Methyl | 0.8 | 0.95 | 0.8 | 0.9 |
| Ethyl | 1.0 | 1.0 | 1.0 | 1.0 |
| n-Propyl | 2.5 | 2.5 | 1.9 | 2.0 |
| n-Butyl | 16.6 | 8.0 | 4.5 | 5.0 |

However I will limit myself, in the further discussion of this subject, to ethyl alcohol only.

*Forms.*—Alcohol is official in the United States Pharmacopoeia in three forms: Alcohol, 92.3 per cent. by weight of $C_2H_5OH$. Alcohol dehydratum, 99 per cent. by weight. Alcohol dilutum, 41-42 per cent. of weight.

To these may be added the various forms of galenical preparations which contain alcohol either as menstrum, solvent or preservative, such as the elixirs, spirits, tinctures, fluid extracts, etc.

The substances from which alcohol is obtained are too numerous to mention. Suffice it to say that almost any carbohydrate, under proper conditions of treatment—fermentation—will yield alcohol. The non-official forms of alcohol (some of these are official in other countries) are:

A. Whiskey. This is obtained by the distillation of the mash of fermented grain, with an alcohol content of from 46 to 55 per cent. (vol.)

B. Brandy (also known as Cognac). A distillate from fermented juice of grapes, with an alcohol content approximately the same as that of whiskey.

C. Wines. (a) White and red wine—according to whether the skin is excluded or included—are non-distilled beverages, the product of fermentation of grape juice, with alcohol content of 10 to 15 per cent. (b) Sherry and port, similar origin to above, with alcohol percentage of from 15 to 25 per cent.

D. Ciders. Fermented liquors obtained from fruit other than grapes. Alcohol percentage, 5 to 10 per cent.

E. Malt liquors, containing, in addition to alcohol (2 to 6 per cent.), more or less sugar, $CO^2$, and hops.

F. Fermented milk, known as kumyss, about 3 per cent. alcohol.

Among the less known alcoholic beverages may be mentioned:

G. Small beer, 1.5 per cent.; brown stout, 6.5 per cent.; bitter and strong ale, 10 per cent.; Chica, or Indian corn beer, a drink of South America; Bouza, or millet beer, also known as murna—used by Crimean

Tartars; Quarî, or rye beer, a Russian drink; ava, cava, or arva, prepared from the root of long pepper; formerly used in the South-sea Islands, all along the Pacific Ocean, Tahiti, Sandwich Islands, and Fiji Islands.

A great deal has been said and written with reference to the constitution of the substances that give wine its flavor. This matter is involved in considerable obscurity and the greatest differences of opinion obtain. According to older writers and investigators there is one aromatic substance present in all wines; this substance is known as œnanthic ether, $C_2H_5C_7H_{13}O_2$. Other aromatic substances present in wine are: ethyl acetate (acetic ether), $C_2H_5C_2H_3O_2$, developed in wine by age and frequently added for the purpose of adulteration to simulate age in wine and to improve the "bouquet." Butyric ether, or rather the esters thereof ($C_2H_5C_4H_7O_2$), and caprylic ether ($C_2H_5C_8H_{15}O_2$), both of which have a fragrance resembling pineapple, are also employed for similar purposes. A variation of the bouquet may also be produced artificially by any of the following ethers: caproic, pellargonic, capric, proprionic, amylic, and many others.

Plants, such as rose leaves, lime and elder flowers, leaves of the meadow sweets, peel of the quince pear, blossoms of wild vines, sage leaves, violet roots, and many others are also used to increase the bouquet of different wines.

According to more modern investigators the different bouquets are dependent upon the differences in the yeasts infesting the grapes. So, for instance, the inoculation of a barley infusion with a wine yeast give the fermented liquid the peculiar flavor of that particular wine.

Generally speaking, we may say that the chief and only difference in the different alcoholic liquors is in the substances from which the mash is made.

Liqueurs, cordials, and bitters, running in alcoholic content from vermouth (17 per cent.) to absinthe and benedictine (55 per cent.), are made by mixing fragrant herbs with alcohol or wine and either macerating or distilling.

*Mode of Administration.*—Alcohol has been administered practically, in every manner known to medicine, excepting perhaps the intravenous method.

*Pharmacology.*—Inasmuch as provision has been made in our symposium for detailed discussion of the effect of alcohol on the individual organs and tissues, I will but briefly touch upon its pharmacological action.

*The Cell.*—Upon the individual cell it acts as a protoplasmic poison, interfering with the oxidation of the tissues and leading to fatty de-

generation. It is also said to diminish the resistance to acute and specific diseases, to lessen phagocytosis, and to interfere with the development of immunity.

*Central Nervous System.*—While alcohol has been considered a stimulant to this system, modern investigation necessarily leads us to a contrary conclusion. We must concede to the brain, the functions of control and inhibition. When, under the influence of alcohol a depression of the higher centers is produced, it can readily be understood that the incoordinate, nonconcentrated, and therefore planlessly exaggerated reactions of the more resistant deeper nerve centers (basal ganglia) will become more pronounced and more prominent. The popular saying that "alcohol loosens the tongue," in my opinion summarizes this in a very concise manner. The phenomena quoted from Horace at the beginning of my paper are clearly the manifestations of a loss of inhibition rather than of cerebral stimulation. The ready flow of unbridled speech, the boisterous, often offensive laughter, readily changed to crying, the sudden bursts of temper or even violence cannot be interpreted otherwise.

On the other hand it has been demonstrated that small amounts of alcohol will increase motor efficiency to a considerable extent. This again has been held by some (Kraepelin and others) to be direct evidence of a stimulating effect, while the opponents (Lombard, Meyer and Gottlieb, and others) bring this forward as an additional proof of inhibition of the higher centers. Schmiederberg sides with the latter group and maintains positively that "Alcohol is not a stimulant but a depressant;" that, "in the mental areas the finer degrees of observation, judgment, and reflection are the first to disappear."

*Nerves.*—Götch, in Schäfer's Physiology, quotes experiments of Piotrowsky on the effect of alcohol on the excitability and conductivity of nerves: Alcoholic vapor caused an initial increase in the local excitability and, to a less extent, in conductivity. This soon changed, the conductivity becoming rapidly impaired before the local excitability diminished; on the cessation of alcoholic vapor, the normal conductivity and excitability were reinstated, the latter returning quicker than the former. The reaction time was also increased by alcohol.

*Respiration.*—A distinct "stimulating" effect on the respiration can be credited to alcohol, probably directly due to stimulation of the respiratory center. The volume of the respiration and, as a result thereof, the quantity of exchanged air are increased; the respiratory increase from alcohol is noticeable even during sleep.

*Circulation.*—If one or two ounces of brandy (about 50 per cent. alcohol), well diluted, be slowly swallowed the pulse is slighty quick-

ened; there may be a temporary constriction of the splanchnic vessels and a slight rise in blood pressure. All this is probably due to the irritating action upon the nerves of the stomach. After absorption it has a paretic effect on the vasomotor system with a resulting drop in blood pressure. The effect is general but is especially marked in the nerves and vessels of skin and muscles, causing a rush of blood to the surface. The vessels lose their thermo-accommodation power and consequently there is a large cooling surface which allows of a rapid lowering of temperature, other conditions being favorable. Because of its direct action as a protoplasmic poison on the muscular fibers of the vessels and its paretic effect on the vasomotor nervous system it has a dilating effect on arterioles and arteries, and a similar, though less marked, effect on the heart itself. This causes a lowering of blood pressure, diminution of systolic output from the heart, and the cardiac energy is wasted, pumping blood into relaxed vessels. The large bounding pulse, with comparatively shorter systole, which gives a deceptive appearance of vigor and force to the circulation, is due to the large wave in the dilated vessels. The venous and diastolic pressure within the heart are temporarily increased. According to Dixon in small quantities and in concentrated form alcohol quickens the pulse, constricts the deeper vessels, increases the blood pressure, especially when the heart action is feeble, and is therefore of great service in fainting. In too large doses he considers it as a distinct depressant to the heart.

*Metabolism.*—Many and conflicting views have been advanced regarding its value as a food, and its influence on metabolism. Neubauer has observed that in severe diabetes mellitus it may be used to check the output of acetone. Atwater and Benedict have shown that the efficiency of alcohol in the protection of body fat is as marked as that of fats and carbohydrates, and somewhat less than its protein saving and protecting power. Experiments have shown that alcohol, prior to its combustion in the body, exerts a notable influence upon the metabolic processes of the liver, and possibly in other organs, whereby a marked effect is produced upon the output of uric acid.

When taken with purin-containing foodstuffs it exerts a direct influence upon the metabolism of those compounds which give rise to exogenous uric acid, increasing largely the amount of uric acid excreted. It therefore cannot be rated as a true non-nitrogenous food in the sense in which fats and carbohydrates are foods.

Experimental: Heart.—After ascertaining the normal rate of the pulse on 62 students the class was divided into three groups: To group 1, no alcohol was administered; to group 2, 4 c.c. of alcohol was given; to group 3, 15 c.c. of alcohol was given. In each case the alcohol was

administered in 120 c.c. of water, group 1 receiving 120 c.c. of water alone, so that none of the students were aware what medication, if any, was administered. Group 3 showed an increase in the rate of the pulse averaging 12.5 beats per minute. Group 2 showed a decrease of the rate averaging 8 beats. Group 1 showed no variation. The effect was noticed within 15 minutes after administration of the drug and lasted for 20 minutes after the first effect was noticed.

Cerebrum.—The same procedure was followed as above, at a subsequent session. The same quantity was administered. Before beginning the experiment three simple mathematical examples were dictated to the students. One example was a simple addition of figures, one a division and the third a multiplication.

At a given signal the students began their work and were again stopped at a signal. Ninety-eight per cent. of the students finished all the tasks and 87 per cent. of those finishing were correct. After a short wait the alcohol and, to group 1 the water without alcohol was administered. Ten minutes after adminisration the signal was given to begin work, three examples exactly similar in every way to those previously given were undertaken and the work stopped as before, within the same time limit. All of the men receiving the alcohol had finished the work in the time allotted. Ninety-seven per cent. of those having received the water were finished. Of those receiving the alcohol the results were as follows:

Group 2 (4 c.c.), 78 per cent. were correct.
Group 3 (15 c.c.), 62 per cent. were correct.

Conclusions: Alcohol caused a quicker response but at the expense of accuracy.

Metabolism.—Four patients with diabetes mellitus were daily examined as to percentage of blood sugar. One showed acetone in the urine and all had an increased blood sugar content. After administration of 4 c.c. alcohol for 8 days the percentage of blood sugar decreased in all patients, the diet remaining the same. The blood sugar (Lewis & Benedict method) ran from 0.135 to 0.413 before alcohol was administered and sank to 0.135-0.168 respectively.

| | Before. | At end of exp. |
|---|---|---|
| Case 1 | 0.182 | 0.135 |
| Case 2 | 0.413 | 0.159 |
| Case 3 | 0.357 | 0.168 |
| Case 4 | 0.284 | 0.162 |

Whatever the evidence of the laboratory may be, however, we must bear in mind that in the final accounting we have to consider this as a

drug and its action in pathological and not under normal conditions. And here the final word belongs to the man who makes his observation at the bedside.

May I therefore quote, as my concluding sentiment, from one of the keenest observers and clinicians, our late Abraham Jacobi, "I do not care to classify alcohol anywhere. I do not contest obervations and experiments on either healthy or diseased men and on animals. . . . One of the most profitable laboratories, however, is the hospital and the private bedside." . . . And there he found alcohol a valuable remedy.

Great clinicians are more circumspect than loud. Hippocrates says more frequently than any of his successors, "It seems to me."

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## THE EFFECT OF ALCOHOL ON THE GASTROINTESTINAL TRACT

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In the discussion of any subject it will be noted that erroneous ideas are due to two principal causes: first, the ignorance of facts, and second, ignorance of the relation of facts to the problem under consideration. Error arising out of gross ignorance is usually compara-

tively innocent and harmless, as compared with that brought about as a result of a misinterpretation or misuse of known facts.

This, I believe, is especially true in the domain of medicine, and more particularly in experimental physiology, pharmacology, and therapeutics. We see experiments made upon herbivora and the deductions applied to omnivora; observations on the normal applied to the abnormal, and vice versa. The voluminous data on the physiological and pathological effects of alcohol on the human organism are no exception to this general statement, but an excellent example. This is so notorious that the discussion of the subject provokes a smile, if not ridicule.

The mention of alcohol brings up ideas concerning its industrial, economic, social, political and sometimes its physiological relations, and last and least of all, its therapeutic application; and in the discussion the ideas become so mixed that the truth on any one point is usually obscured or missed altogether. It is, therefore, especially necessary that one should be very explicit in stating what aspect of the subject is to be discussed and in what domain the deductions are to be applied.

The title, "The Effect of Alcohol on the Gastrointestinal Tract," should convey the following definite ideas: 1, Therapeutic preparation; 2, therapeutic doses; 3, administered in disease; 4, diagnosed by a physician.

This should exclude many data and many ideas which have no bearing on the aspect of the question under discussion, but it does not always do so, for we see advocated the proposition that alcohol should be excluded from the pharmacopeia, and the reasons given such that, if valid, they would be equally applicable to such drugs as mercury, bromide, belladonna, and opium; for mercury in large doses is an irritant to the gastrointestinal tract, kidneys, liver, and central nervous system; bromide impairs mental accuracy and physical efficiency; belladonna in large doses will produce an active, talkative delirium, and opium is a habit-forming narcotic.

Although some of the physiological experiments have been made with pure alcohol diluted with water, it is needless to state that it is practically never used internally for therapeutic purposes in this form, but as wines, beer, brandy, whiskey, liqueurs, and cordials and as a solvent for various drugs.

Taking up the effects on the digestive tract in the order in which they are produced, we have first the sensory effects. Here at the very beginning we are face to face with specific application of a fact of fundamental importance and general application, namely, that it is impossible to discuss therapeutics intelligently without referring to physiology, for it is through sight, smell, taste, and physical contact

that alcoholic preparations produce their sensory effects on the digestive tract which must be summed up under the term appetite.[1] Now, appetite and hunger are not, as many suppose, different degrees of the same sensation. They are fundamentally different; that is, they differ in quality, for hunger is essentially an epigastric sensation of varying degrees of discomfort or pain, definitely associated with the characteristic hunger contractions of the stomach, while appetite for food is a much more intricate complex, an emotion.

While a certain sensation complex from the viscera and an approximately normal state of central correlation constitute a necessary background for the development of appetite, the condition itself is essentially a complex psychic state, or emotion, aroused by the action of sensory stimuli having pleasant memory associations with past experience.

To describe the steps by which a sparkling glass or foaming mug stimulates the appetite would be pedantic. The increased flow of saliva and the swallowing movements induced by visual memory alone speak convincingly. The stimulation of the olfactory nerves by the aroma acts in a similar manner, no less effective.

The taste of pure alcohol, or the same diluted with water, is not especially appetizing, but the alcoholic beverages containing aromatic substances from the grapes, ethers, esters, etc., or the malt drinks act through the end organs of taste to increase appetite.

The physiologist Carlson states:[2] "The writer is neither a total abstainer nor a habitual user of alcoholic beverages. But it is his experience that a glass of beer taken at meal time seems to awaken or increase appetite. The effect is rather immediate and therefore not due solely to the absorption of the alcohol. Pavlov has recorded an instance from his own experience where a drink of wine seemed to initiate the sensation of hunger the very minute the wine reached the stomach."

In addition to the above mentioned action of such beverages through sight, smell, taste, and directly on the gastric mucosa, there is another important method of action.

Hunger may be present with all its qualms, and accessory phenomena of lassitude, weakness, nervous irritability, and vasomotor instability without appetite for food. Unpleasant emotions, anxiety, depression, or mental fatigue usually inhibit the appetite even when hunger and need of food are present. Under such conditions a moderate dose of alcohol when absorbed acts on the higher psychic centers in such a manner that inhibition is relaxed, the emotions released, and there is a pleasant physical and mental relaxation with a feeling of ease and comfort during which inhibited appetite returns. Overdosage may destroy

appetite just as overeating of the most harmless food will produce a feeling of revulsion, and even digestive disturbance or disease.

On the secretory function alcohol causes a temporary increase in the outflow from the glands, but no permanent increase in production.[3] It is therefore a negligible factor in its action on the secretion. After absorption, even from the rectum, it increases gastric secretion.

On the ferments, minute quantities, not over 2 per cent., slightly accelerate the action under experimental conditions. Larger amounts, of from 5 to 10 per cent., slightly retard proteolytic action.

Foods are unaffected in the stomach, with the exception of proteins, which are coagulated or precipitated if in solution, which is a preliminary step in digestion.

In the preparation of foods, especially eggs, milk, and sauces, it increasess their palatability and digestibility and adds to their nutrient value.

Alcohol and alcoholic solutions are absorbed from the stomach more rapidly and to a greater degree than any other substances.[4] The rate of absorption depends very greatly upon the amount and character of other substances present in the stomach. For example, milk is the most effective foodstuff for delaying the absorption of alcohol into the blood, and this is almost equally effective whether mixed with the alcohol at the time of drinking, or drunk two hours before the alcohol. Fats inhibit its absorption, especially when in strong solution. Other foods have very slight effect in this respect.

The relative amounts of alcohol absorbed from the stomach and the intestine naturally vary very greatly with such conditions as the character and amount of foods in the stomach and the rapidity of evacuation. This is, however, a matter of little practical importance since the drainage in each case is to the liver.

On the motor function of the stomach it acts as a carminative, that is, it arrests or modifies excessive contractions, without inhibiting normal motility. As a result of his most accurate experiments on the motor functions of the stomach, Carlson states:[2] "Tests were made with sour and sweet wines, brandy, beer and pure alcohol diluted with water. * * * In view of the fact [already stated, that alcoholic drinks promote appetite] we expected to find that these alcoholic beverages increased the tonus and the contractions of the empty stomach, since it is the tonus and the contractions of the empty stomach that give rise to the hunger sensation. To our surprise the results proved to be the very opposite. Wine, beer, brandy, and pure alcohol (diluted) introduced directly into the stomach inhibit the hunger contractions and the tonus

of the empty stomach instead of increasing them. * * * In other words, alcoholic beverages when introduced directly into the empty stomach in quantities and concentrations that directly affect the tonus and the contractions of the stomach cause inhibition, and inhibition only. * * * The duration of the alcohol inhibition varies directly with the quantity and concentration of the beverage introduced into the stomach. Thus, 50 to 100 c.c. of 10 per cent. alcohol may inhibit the hunger contractions for 1 to 2 hours; or, if introduced during a period of relative quiescence, it delays correspondingly the onset of the next hunger period. Inhibition for 30 to 60 minutes is caused by 200 c.c. of beer. The sour wines on the whole cause greater inhibition than the sweet wines, probably through their acids. * * * If alcoholic beverages in the stomach caused as marked inhibition of the stomach movements in digestion as they do in the stomach movements in hunger, even moderate drinking with meals would lead to acute indigestion. As this is not the case, it is evident that alcoholic beverages affect the mechanism of these two types of movement differently."

The unpleasant emotional states of anxiety, depression, or mental fatigue which inhibit appetite have been shown by both experiment and clinical experience to impair gastric motility. Under such conditions alcohol absorbed acts upon the higher nerve centers, producing inhibition, relaxation, and mental ease, with resulting improvements in the gastric condition and restoration of normal motor function.

From the facts presented and their relation to human physiology, it is a reasonable deduction that alcoholic beverages have certain practical application in the treatment of diseases in which it is desired to influence the gastrointestinal tract. Therapeutic use and contraindication must be determined here as elsewhere by the physician who has diagnosed the particular case, but a statement of certain principles, with examples of application may be given.

In any case where it is desired to awaken or stimulate the appetite, one of the wines or malted drinks would be an aid, and the dose of the beverage used for such a purpose would not contain a sufficient quantity of alcohol to fall under any of the contraindications hereafter mentioned.

In conditions of hypermotility of the stomach, due to mental unrest, anxiety, or worry, accompanied by a feeling of epigastric discomfort, fullness, and distention or tightness, alcoholic beverages, as above stated, act both locally and after absorption on the mechanism involved; namely, inhibiting excessive contractions when introduced into the stomach, and when absorbed acting on the central nervous system, producing psychic relaxation, which, if not removing the cause, at least makes it ineffective.

While a drink of whiskey or beer will allay the pains of gastric ulcer

or pylorospasm, its use in these conditions as well as in all other conditions requiring surgical treatment is not rational.

Alcoholic beverages should not be used as a stimulant in cases of nausea, vomiting, and shock when the condition may be due to the presence of unknown toxic substances in the digestive tract, because they generally increase the absorption of certain substances and would therefore increase the systemic effects of the poison.

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## EFFECT OF ALCOHOL IN THE THERAPY OF INTERNAL DISEASES

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It is probable that over the action of no single therapeutic agent has there been more acrimonious and combative discussion than over that of alcohol, owing to the contentions arising from its use as a beverage. This paper seeks to avoid the discussion of alcohol from any other than the therapeutic standpoint and as relates to general disease.

As a remedy, probably it has been more widely employed than any other agent, and until recent times the great importance of this use was unquestioned. The action looking toward the exclusion from the pharmacopeia of alcohol as a remedy probably fails to represent the opinion of the majority of physicians. The action of the House of Delegates of the American Medical Association on this subject makes it advisable for the American Therapeutic Society to review the subject thoughtfully, avoiding if possible the acrimony which heated debate often engenders.

A conservative examination of the question is convincing that any substance so potent as alcohol, used so widely and indiscriminately in the treatment of all manner of diseases and symptoms, must necessarily have been harmful to many. Its supposed happy effect in many instances results from its dulling influence upon the nervous system and the temporary relief to mental and physical suffering. All will admit that to

obscure a symptom is not necessarily desirable. Also it will be conceded that to charge the metabolism with the burden of dealing with assimilation and dissimilation of alcohol may at times prove an embarrassment to physiological activity and be a source of injury to the parenchyma of organs. Because of these and other possibly harmful effects, it has been asserted that alcohol is always a poison, and has no place in legitimate medicine. That such a decision is inconsiderate, partisan, and unsafe, I think there can be no doubt. The arguments advanced against the therapeutic use of alcohol might be raised as justly against the employment of any really powerful drug. Because it is competent to do harm is no reason that it is not competent to do good.

*Alcohol as a Nutrient.*—In considering its field of usefulness in general medicine, we cannot omit its importance as a substitute for food. By giving alcohol we often tide the patient over a critical period when other means of sustenance fail. To deny this is unreasonable. This is true in gastrointestinal diseases when there is faulty assimilation. When from exhaustion the digestive apparatus is so far crippled that it cannot digest or absorb the required amount of other forms of food, the administration of brandy, whiskey, or wine will save life, and to omit it approaches criminal neglect.

In diabetes, when it is incumbent to lessen the caloric intake of carbohydrates or of fats, or of both, alcohol in a certain class of cases serves an excellent purpose; nothing else can replace it. This is true at times in acidosis not related to diabetes.

*In old age,* when the organs have undergone degeneration from senility, so that there is loss of vitality and functional power, there can be no doubt of the very great importance of alcohol. Used judiciously and with the same care which is exercised in the prescription of other drugs, alcohol often enables an aged person to live on, not only with greater functional power, but with comparative satisfaction. Thus the patient is spared misery of mind and body, and the moral atmosphere of the home is improved. Careful and elaborate studies in nutrition may guide us to accomplish a great deal without the assistance of alcohol, but a satisfactory result may be more easily obtained by having recourse to it, and at times the benefit which follows its regulated administration can be attained by no other means.

*In Typhus and Typhoid Fever (Collapse and Convalescence).*—In a recent interview published in the *New York Times* (Feb. 20, 1921), Dr. Stephen Smith describes his experiences as an intern working under Alonzo Clark, in the successful treatment of typhus fever by the very liberal employment of alcohol, especially brandy. The success attained through this treatment according to Stephen Smith was extraordinary,

and no other measure could compare with it. No one is likely to doubt the wisdom which Alonzo Clark showed in therapeutics, and every one acknowledges the perspicacity of Stephen Smith. Personally I know nothing of the treatment of typhus fever, but there is in this contribution the awakening of a forgotten truth that should be welcomed at this time. As to the value of alcohol in the routine treatment of typhoid, I am in doubt. Having lived through the time when it was generally employed and through a later period when it was excluded, I am unable to come to a definite opinion regarding the question. However, in stages of collapse and in the period of convalescence, alcohol is undoubtedly of value. This observation applies to a wider field than typhoid fever.

*In Influenza Pneumonia*, in certain phases of other types of pneumonia, alcohol in my judgment is of great value.

*Infections.*—In grave depression accompanying erysipelas, diphtheria, cholera, cholera nostras, dysentery, and other infections, alcohol may be regarded as of very real value as a substitute for food and as a definite stimulant. Of course it is of alcohol as a temporary remedy, thoughtfully administered, that I speak; when used to excess and habitually it undoubtedly predisposes to infection, through lowering of immunity.

*In Chronic Diarrhea*, where there is hyperperistalis, such as occurs in achylia gastrica, amyloid infiltration, tubercular enteritis, in some types of dysentery and in various other local infections, a properly selected alcoholic preparation not merely gives comfort to the patient, but at times is positively a life-saving agent for which there is no satisfactory substitute.

*In Diseases of the Circulatory Apparatus* alcohol in moderate doses dilates the blood vessels, especially the superficial ones, and according to the U. S. Dispensatory (20th Edition) "increases the amplitude of cardiac action." With these established facts in mind it is understandable why alcohol has become the familiar companion of the victim of angina pectoris. In cardiac insufficiency, especially when the capillary area is narrowed, alcohol is of great value. Here it should be employed in rather frequent small doses, so that it can be completely oxidized and so that its action upon the capillary area may be utilized.

*In Nervous and Mental Diseases* alcohol, although formerly widely employed with and without professional sanction, has come to be used most guardedly. The objections to its use are evident, and yet there are instances in which it is of very great value. In the depressive psychoses, psychasthenia, and in exceptional cases of neurasthenia, alcohol is at times of value. Its well known predilection for nerve tissue leads the observant physician to be wary of its effects. Many individuals

have a remarkable susceptibility to the action of the drug. When used but moderately by such persons there is set up nerve irritability or even polyneuritis.

*In Exposure to Cold* alcohol acts quickly to restore the circulation and to restore vitality, especially when the subject is placed in a warm room. On the other hand, it diminishes resistance to cold, and when taken before or during exposure to a low temperature, it blunts consciousness, impedes physiological reaction, leads to internal congestion, invites infection, and is generally mischievous.

*In Convalescence* alcohol preferably should be given in the form of a suitable wine, and its administration carefully guarded by the physician to avoid the well known habit-forming tendency of the drug, especially when the patient belongs to the type of which inebriates are made. Long before the patient is dismissed alcohol should be discontinued and replaced by scientific feeding and psychotherapy.

Alcohol should not be given in quantity greater than that which the organization can readily oxidize. The physician must act as the censor and educator when prescribing the drug, somewhat as with opium or hypnotics. Needless to say, the popular use of alcohol as a preventive and remedy for nearly all illnesses and in case of injury should be most strongly condemned. The harm from the thoughtless employment of this agent has led to its opprobrium.

Finally, it is held that alcohol is an important, sometimes indispensable remedy, that it should be included among the drugs in the Pharmacopeia, that it should be prescribed with discrimination and with a full sense of responsibility, without prejudice, and with careful record of results. The present legal restrictions to the therapeutic employment of alcohol place upon physicians an unnecessary burden and add perplexity to our efforts in relieving human suffering.

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# THE EFFECT OF ALCOHOL ON THE HEART AND BLOOD VESSELS

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The clinical relation of alcohol to the heart is not at all a close one. It cannot be said that alcohol has any direct or immediate effect in producing heart disease. Indeed, alcohol presents a social problem far more than one pertaining to health. Just as the law which compels school children to gaze upon diagrams of stomachs turned purple by alcohol is ridiculous, so it is absurd to attempt to build up a case against alcohol on the basis of the production of organic heart disease.

It needs no argument to procure a conviction of the moral, economic, and mental deterioration which results from the abuse of alcohol, but no one has yet been able to prove that alcohol, divorced from the usual unhygienic accompaniments of the abuse of alcohol, has ever led to organic heart disease. That it results in arteriosclerosis has been disproved by the dissection of many drunkards, dead of pneumonia or other infectious disease.

The great fundamental cause of premature arteriosclerosis in the overworked business man is undoubtedly often founded on the reflex action of worry upon metabolism, and it is more than likely that the moderate use of alcohol at the proper time of day and in the proper quantity, removing as it does this nervous and mental tension and abolishing worry for the time being, may be indeed a preventive of arteriosclerosis.

No one will maintain that alcohol can result in organic valvular disease. As to myocardial changes observed in excessive beer drinkers, it may be said that this has to do in all probability much more with the excessive intake of fluid than with the actual alcoholic content of the beer.

To quote some authorities:

1. One authority says: The extremists, who find no good whatever in alcohol, hold that it is a fallacy to apply the term "stimulant" thereto; that alcohol is a paralyzant from first to last; that its apparent cardiac stimulation is in reality the result of its narcotism of cardiac inhibition; and that every special sense is blunted by even small doses of this poison. They calmly ignore the fact that their premises apply to every stimulant in its special field of action as well as to alcohol in its sphere, and forget that their conclusion (that alcohol has no

place in medicine except as a poison) applies by the same reasoning to every other stimulant. Hence, to be consistent, they should advocate the banishment of all stimulant drugs from the materia medica.

2. Another says: In heart disease very little alcohol, either as wine, or as brandy or whiskey, may be allowed to persons accustomed to its use. Beer is less advisable, since it carries with it large quantities of liquid and often disturbs the digestion as well, whereas, wine, whiskey, or brandy in small quantities improves it. Against this is balanced the deleterious effect of alcohol upon the heart muscle. Large quantities tend to produce fatty degeneration of the latter. Whether small quantities have any such effect in the individual case is uncertain, but it must be borne in mind that the injured organ is much more susceptible to deleterious influences than is the healthy organ. It is a safe rule that, in persons not already addicted to its use, brandy or whiskey be given only in doses which serve as carminatives, and not in doses intended for stimulation. Even the psychic effect may often be secured as well by small doses as by large ones. One point in favor of alcohol in man as against animal experimentation lies in the fact that in such persons it greatly increases the sense of well being and removes psychic depression and worry. The latter may be especially straining upon the heart, and hence every effort should be made to ward it off, especially during certain crises; but it should be borne in mind that the patient may easily become dependent upon the drink to arouse his spirits, and in this state more harm than good is done. The greatest judgment should be used in the administration of alcohol even in small quantities, and it should even then be reserved for crises when the stimulation of every fiber is all-important. On the other hand, alcohol should never be withdrawn suddenly from persons addicted to its use, since this procedure often precipitates an attack of delirium tremens, but moderate doses (whiskey 15 c.c. or ½ oz. every four hours) should be given.

3. Another says: Palpitation and the other symptoms of "cardioneurotic" (pseudocardiac) weakness also occur in persons who take alcohol in quantities that are just in excess of their tolerance, and the possibility of this cause must be borne in mind. In some individuals, palpitation and irregularity may follow the ingestion of a single glass of wine, without any symptoms of intoxication setting in. That these conditions may continue without the patient's recognizing the cause is a common experience, and a considerable number of cardioneurotic cases result from this unintentional over-indulgence in alcohol. Women and young persons are more sensitive than men. The functional power and endurance of the heart muscle is, moreover, weakened by alcohol; and acute dilatation may set in from comparativey slight exertion. If the use of alcohol is long continued, it may lead to fatty and fibrinous myocardial change, but this in mild cases subsides when the cause is removed.

4. A writer on the heart says: The degree of damage to the cardiovascular system by alcohol is still a matter of dispute. Like other poisons, it affects the cardiovascular structures to a variable extent, so that necropsy reports showing absence of cardiovascular damage in chronic alcoholism are not necessarily evidence of its innocuousness. It is probably true, however, that the importance and frequency of alcohol as a cardiac poison have been overestimated. Alcohol attacks particularly the cardiac musculature; the result is myocardial disease varying from slight fatty degeneration to scar-tissue formation. The arterial sys-

tem, when attacked, presents various grades of intimal thickening and calcareous deposits, and, in exceptional cases, degeneration of the remaining arterial coats. . . . In animals, alcohol slightly increases cardiac contractility. In human beings, when given in large quantities, it produces a marked fall of blood pressure by its action upon the vasoconstrictor center and upon the heart muscle. Small quantities of alcoholic beverages seem occasionally to augment cardiac contractility in decompensated cardiac disease, but the effect is slight and inconstant, and its value problematical. . . . There are certain factors which require brief comment because of their influence upon blood pressure. Moderate amounts of alcohol do not regularly raise the blood pressure in man. In the experimental animal, large doses produce a fall in blood pressure, due to an effect upon the vasconstrictors and upon the heart.

5. The latest book on Heart Disorders that has come to my desk says: Alcohol raises for a few moments the systolic pressure, and thus acts as an apparent circulatory stimulant; it cannot, however, be regarded as a true circulatory stimulant, inasmuch as it decreases cardiac efficiency, raises disproportionately the diastolic pressure, and lowers pulse-pressure, according to the exhaustive investigations of Lieb, corroborated by many others. Alcohol is no longer considered a food, for it has been determined that its oxidation (as is that of uric acid, xanthin bodies, leucin, etc.); it is not oxidized for the purpose of being used by, or stored up in the economy, as a food.

I take it that this discussion is not from the point of view of alcohol as used in the community. As a therapeutic measure, the use of alcohol has undoubtedly served a very valuable purpose in the past as a sedative, particularly in fevers of the typhoid type. It is also necessary to prevent the development of withdrawal symptoms in those who have been previously accustomed to the use of alcohol. This use, of course, under prohibition will need to be employed less and less.

I have never found it desirable or necessary to prohibit the moderate use of alcohol in people suffering from heart disease or arteriosclerosis. In this I find myself in agreement with English authorities, and only out of touch with those of the profession who for some reason or other have been led to believe that alcohol was the cause of organic disease.

A very sharp distinction should be made between the use of alcohol and profound alcoholic poisoning, such as is observed in a person who drinks to the point of coma. In the latter case the extreme physiologic effect of alcohol is observed and manifests itself in a condition resembling shock, with a low blood pressure, cold and clammy surface of the body, and profound stupor. Even so, the circulatory organs have not received any particular damage, the brunt of the poison falling upon the nervous system.

The other question that will arise in these times is whether alcohol is necessary and desirable in the treatment of heart and circulatory diseases and the answer is that there are many better remedies to ac-

complish any desired effect, but alcohol has often proved a convenience in the relief of angina pectoris or physical collapse because it was ordinarily quickly available. Nitroglycerin and aromatic spirit of ammonia can fulfill every requirement and fulfill it better than alcohol, but in former times one could obtain alcohol where the others were not obtainable.

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## THE EFFECTS OF ALCOHOL UPON THE ENDOCRINES

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No one, perhaps, more keenly than the medical man recognizes the misery, neglect, starvation, brutality, disorder, crime and pathological processes which, directly or indirectly, are attributable to the abuse of alcohol. In our efforts to assist in overcoming so deplorable a state of things, however, we should not overlook the responsibilities incumbent upon us as legitimate arbiters in matters concerning public health, mental and physical. Particularly does this apply to a question upon which depends to-day a decision of great moment to the welfare of the entire nation, that pertaining to the actual meaning of the word "intoxicating" as applied to alcoholic beverages, left undetermined in the 18th Amendment. In fulfilling our mandate in this connection, however, we should avoid an attitude of mind which is bidding fair to annul and degrade for the future any effort in favor of true temperance, the only line of conduct compatible with the rights and best interests of a free people. By this I mean temperance in all things, just as much in carrying out prohibitive laws as in the use of alcohol itself. Briefly, we should avoid all partisanship, and particularly that pernicious trend too often encountered nowadays even among well-meaning people, fanaticism—a form of obsession in which the mind, by becoming the abject slave of its prejudices, loses all sense of proportion and justice.

Last year, in the Presidential Address before this Society, I sub-

mitted evidence to the effect that it was through the endocrines that many of our most efficient drugs and other agents produced their beneficial effects and, when used in excess, some of the phenomena we group under the term "tonic effects." This conception of drug action, the foundation of which was first laid in 1903 and 1907 in my work on the "Internal Secretions," applies likewise to alcohol, and elucidates several admittedly obscure points concerning the pharmacology of this agent. To convey at all clearly, however, the bearing of this statement, it is necessary to review succinctly the functions of those endocrines which are known to be influenced by alcohol.

Beginning with the adrenals, it is believed by many that confusion exists concerning the functions of these organs. Thus, while in 1894 Oliver and Schäfer found that adrenal extract raised the blood pressure, other physiologists showed that it lowered it, particularly when small doses were used. Again, Abelous and Langlois having found that the adrenal hormone possessed antitoxic properties, other physiologists failed experimentally to discern any such action. Even Cannon's familiar emergency theory in which emotional stress—fright, excitement, etc.—is adduced as a cause of excessive functional activity, has been held by others to be fallacious.

All these functions are harmonized, however, when interpreted in the light of a fundamental function I found the adrenals to possess, which was that their secretion sustains respiration and metabolism by supplying the hemoglobin with the substance which enables it in the lungs to become converted into oxyhemoglobin. This view, confirmed by others since it was first formulated in 1903, sustains Oliver and Schäfer's observation that the adrenal secretion raised the blood pressure, since the relatively large doses they used increased greatly the oxygenation and metabolism in the muscular tissues of the heart and blood-vessels, and caused them to contract. Even moderate doses may cause a rise of blood pressure by acting directly upon the first tissues affected by the adrenal principle, the non-striated fibers of the arterioles. These terminal arteries, by contracting, then increase the vascular tension behind them and raise the blood pressure. The apparently destructive observation of Moore and Purinton that minute doses of adrenalin cause dilatation of the arteries also finds its normal explanation, for such doses first contract the vasa vasorum, owing to their minute caliber. These diminutive vessels, supplying as they do, arterial blood to the muscular coat of the larger vessels, cause, when contracted, dilatation of the latter, thus lowering the general vascular tension and the blood pressure. The antitoxic theory of Abelous and Langlois is also readily accounted for in this process, since increased oxygenation and

metabolism tend normally to enhance defensive efficiency, while subjects in whom, as in Addison's disease, the adrenals are the seat of organic lesions, are known to be very vulnerable to infection. Finally, Cannon's emergency theory also becomes a normal feature of increased oxygenation and metabolism since the needs of efficient defense require the increased adrenal activity observed by this physiologist.

Turning now to the physiological effects of alcohol, Sollmann[1] writes, referring to its action in moderate doses, typical of stimulation*: "There is an increase in the rate of the *respiration* and of the *heart;* the *blood pressure* rises." He states, moreover, that "stimulant" doses of alcohol also increase markedly "the rate and depth of the respirations" and that "the amount of respired air may be doubled." All these phenomena are typical of increased adrenal function. They are produced, moreover, not only by small doses of alcohol but are also sustained for a time by the prolonged use of alcohol. Does alcohol, however, stimulate the adrenals directly? This was shown by the researches of Bernard and Bigart,[2] who found that slight intoxication increased their functional activity; Aubertin[3] also found in experiments on animals that even chronic alcoholic intoxication caused hyperactivity of the adrenals, with marked hyperplasia. In one of two cases of marked chronic alcoholism studied by Schmiergeld,[4] the adrenals showed changes in the spongiocytes of the glomerular layer which likewise indicated hyperactivity. That these phenomena are brought about by stimulation of the respiratory centers which include that governing the adrenals, is also shown by many experimental facts including the observation of Burge[5] that alcohol greatly increases the catalase of the blood. This catalase is, as my own researches have shown, the adrenal ferment adrenoxidase, thus indirectly sustaining all other observations that alcohol stimulates the adrenals when administered in moderate doses.

Conversely, when large doses are ingested or chronic alcoholism due to the continuous use of large quantities of alcoholic beverages prevails, the functional activity becomes deficient. Thus Bernard and Bigart[2] and also Aubertin found in such cases cellular lesions corresponding with those of hypoadrenia. These effects have likewise been noted by other observers. E. F. Hirsch[6] has also called attention to marked alterations in the cortices of the adrenals in cases of delirium tremens.

On the whole, what observations have been made on the effects of alcohol upon the adrenals show that when employed in therapeutic doses as a stimulant, or used daily in moderation, it promotes the functional activity of the adrenals and therefore general oxygenation and metabolism. This fully supports the observations of Sollmann[1] who states (p. 554), after reviewing the pharmacological domain on the subject that *"it may*

*be considered as probable—some authorities to the contrary notwithstanding—that a certain amount of alcohol (variable in individual cases) may be taken daily without any demonstrable permanently injurious effect.*" Conversely, it is equally certain that what has very properly been described popularly as "intoxication" and chronic alcoholism tends to cause pathological lesions in the adrenals which may compromise temporarily or permanently, their functional efficiency.

Other factors bearing upon the relationship between alcohol oxidation and the adrenals will be considered presently.

Turning to the thyroid, the fact that this organ is also concerned with metabolism needs only to be recalled. Kendall,[7] who isolated thyroxin, its most active principle, states in this connection: "The changes occurring in a patient with thyroid deficiency, or in experimental animals by the administration of thyroid are so great that practically every cell within the animal organism is changed. The effects are felt throughout the nervous system and the circulatory system, the rate of metabolism is enormously increased and even the skin and hair show revolutionary changes." Moreover, we also find the thyroid concerned with defensive functions. While Victor Horsley in 1892 found that the rôle of the thyroid in catabolism included the breaking down of toxic waste products, my own labors published in 1903-1907 showed that the thyroparathyroid hormone took part in our defensive functions against infections and exogenous pathogenic agents, the hormone constituting what Wright and Douglas have since termed "opsonin." This has been repeatedly confirmed in Europe. McCarrison,[8] who has himself contributed much to our knowledge in this connection, states in a review beginning with my labors in 1902: "The fact that the antitoxic and bactericidal resources of the body are largely dependent on the functional perfection of the thyroparathyroid mechanism is, I believe, as clearly established as is the influence of this mechanism on metabolism."

What is the influence of alcohol upon the thyroid? The literature of the subject virtually repeats, in respect to this organ, the statements made concerning the adrenals. As stated by Lorand, small doses of alcohol, particularly in weak solution, do not injure this gland, while stimulating it. In a personal practice covering over forty years, twenty of which have been devoted entirely to endocrinology, I have never seen a case in which, even under the influence of moderate daily use of alcohol, the thyroid showed, during life, at least, any sign of functional deficiency. Conversely, the fact that it is stimulated is emphasized by the observations of several investigators to be mentioned later, showing that therapeutic on non-toxic doses increased the defensive efficiency of the body against disease.

As soon, however, as the line of demarcation between the moderate therapeutic or stimulating dose—which, of course, varies greatly in different individuals—is passed and toxic doses are ingested habitually, the whole picture changes. As emphasized by Hertoghe,[9] de Quervain,[10] Sarbach,[11] and Petroff,[12] degenerative lesions, in which sclerosis is a prominent feature, are produced, with all their evil consequences upon the health of the drunkard, including his own vulnerability to disease and what is worse, upon his offspring. Schmiergeld,[4] in describing the histological lesions found in the thyroids of two confirmed drunkards, which showed marked sclerosis, large bands of connective tissue subdividing the organ into many lobules, etc., states that we cannot attribute the changes strictly to alcohol since they may also be caused by tabes, epilepsy, syphilis, etc. The fact remains, however, that alcoholism may be included among the disorders which cause sclerosis of the endocrines in general. Schmiergeld also found sclerosis in the pituitary of his two cases. This is well illustrated in a microphotograph of the pituitary of a confirmed drunkard shown opposite page 1332 in my work on the Internal Secretions.

The morbid effects of chronic alcoholism upon progeny, so well established by a multitude of recorded facts, has also been placed on a solid footing by the labors of Bourneville, Robinovitch, Bernard, Vincent, LeClerc[13] and others, cretinism being the main disorder observed in the offspring. As this endocrinopathy is the most advanced stage of hypothyroidism, it is probable, as my own observations have tended to show, that a far greater proportion of cases of feeblemindedness and backwardness in children than 5 per cent. (which is the proportion of true cretinism among such cases), may be traced to chronic alcoholism in one or both parents. As to its effects upon progeny through the gonads, Simmonds,[14] Kyrle and Schopper,[15] Arlitt and Wells,[16] nd others found that alcoholism, also the injection of alcohol in animals, caused practically always changes in the testes, resulting mainly in aterations in spermatogenesis. This appears to be the main effect produced, changes in the ovaries being slight or nil, although sclerotic changes are occasionally found. This analysis of the effects of alcohol upon the endocrines, which effects correspond with those upon other organs, demonstrates also that alcohol in keeping with other powerful tonics, strychnine for instance, stimulates functional activity when administered in therapeutic or moderate doses, and that it becomes an active, destructive toxic when taken in large doses.

Besides the stimulating action of alcohol on the endocrines, however, another factor must be taken into account, to wit, the familiar fact that alcohol is oxidized in the blood and tissues. Now, both the adrenal

and thyroid hormones, we have seen, influence powerfully both oxidation and metabolism. How does the oxidation of alcohol square with these glandular functions?

An important therapeutic resource asserts itself in the use of small doses in this connection, while, conversely, large doses find therein an additional power for harm. In the case of small doses, oxidation of the alcohol supplies heat energy to all tissues which is *added* to that produced by its stimulating action upon the adrenals, causing them to unite their efficiency. This parallelism shows itself when they are compared. Thus, Sollmann[1] describes as "stimulant effects" after taking moderate doses of alcohol, an increase of the rate and depth of respiration, the increase in respired air being sometimes doubled, with increase of the systolic blood pressure, particularly where this is depressed, and increase of heart action. In Sollmann's own words, "The amplitude and force of the pulse; the mass movement of the blood; the output of the heart and the efficiency of the circulation in general, will be improved. The effects are not very great and not altogether constant in normal individuals, but they suffice to produce decided therapeutic effects especially in conditions of exhaustion."

This corresponds precisely with the action of adrenalin. Its effects are inconstant and often *nil* in the *normal* individual, but we know that it is also in exhaustion when the vascular tension and the blood pressure is low, particularly at the close of acute infections, that it produces its best effects. Alcohol, through its own property of becoming oxidized and its stimulating action on the adrenals, which itself promotes oxidation, thus combines to form a double source of heat energy and of metabolic activity, culminating in powerful general stimulation towards normal efficiency.

As soon, however, as the therapeutic dose, say 15 to 20 c.c. well diluted, is exceeded, the toxic phase of alcohol begins. This is due to the fact that while a small dose takes up but a small proportion of the body's asset in oxygen, which is readily replaced by an increased intake of this gas, a large dose takes up a greater quantity, more than can be replaced and finally becomes oxidized in part at the expense of the tissue cells including those of the endocrines. Hence, after a period of excitement, the increasing loss of control over the limbs, and when the dose has been sufficient, the total loss of muscular power, etc., which constitutes the "dead drunk."

Another important distinction between therapeutic and toxic doses of alcohol asserts itself when it is recalled that both the adrenals and the thyroid take an active part in the defensive processes against infection. Since, as we have seen, alcohol in therapeutic doses stimulates these

organs, it should in such doses increase defensive activity, while, conversely, large doses which depress these glands should lower defensive activity. This is precisely what independent observation has demonstrated. As far back as 1903, Hobart A. Hare[17] found as the result of a comprehensive study, that alcohol combated infections by increasing the bacteriolytic power of the blood when administered in ordinary medicinal doses. This corresponds with the observations of Müller,[18] Wirgin,[19] Parkinson,[20] and others. Parkinson's experiments showed, moreover, that while small quantities of alcohol temporarily increased the production of antibodies, large doses caused the opsonic index to fall. If these large doses were persisted in, the opsonic index remained low permanently indicating failure of the defensive mechanism. The protective value of small doses of alcohol in free dilution was also illustrated repeatedly during the world war. Conversely, the predisposition of the drunkard to infections and the unfavorable prognosis chronic alcoholism entails in these diseases are too well known to require emphasis.

Finally, as is well known, the benefits derived from the moderate use of alcohol manifest themselves mainly in the direction of recuperation after great fatigue, during convalescence from debilitating diseases, or in the debility due to old age. This also coincides with the main indications for adrenal preparations—a suggestive fact in view of the stimulating action of therapeutic doses of alcohol upon the adrenals previously mentioned. During the war it was found by Josué,[21] Satre and Gros,[22] and others, that overstrain in troops, with symptoms of cholera (Asiatic cholera having been shown by myself in 1903 to correspond symptomatically with complete adrenal failure, a fact also confirmed during the war by the remarkable effects of adrenal injections) was promptly arrested by the use of adrenalin. While alcohol has long been our sheet anchor in the threatening heart failure often witnessed at the close of acute infections, we now know that intramuscular injections of adrenalin in 8-minim doses of the 1-1000 solution has the same effect while acting more promptly. In the aged, atrophy of the adrenals is now fully recognized pathologically and clinically as an underlying cause of their weak heart and circulation. Ample experience has shown that the moderate use of alcohol is of great value in the elderly—doubtless due to its stimulating action on the adrenals. The workingman after a hard day's labor experiences great relief and a sense of well-being from a couple of glasses of beer or wine which, by stimulating his endocrines, his systemic oxidations, and his circulation, aid in the catabolism of fatigue wastes. Known as these wastes are to breed bad temper and irritability, the temperate use of such stimulation, by creat-

ing a sensation of comfort and well-being, replaces these elements of family trouble by geniality and cheerfulness, which make for good fellowship. Again, does science confirm biblical text:

He causeth the grass to grow for the cattle, and herb for the service of man that he may bring forth food out of the earth, and *wine that maketh glad the heart of man.* Psalm civ, 14, 115.

As to the dilutions of alcohol which prove harmless even in large quantities, the consensus of opinion among pharmacologists is well summarized by Sollman who, after reviewing its effects upon the mental attitude, the circulation, the digestion, etc., states that "alcohol should be taken well diluted as light wines or beers." The more recent investigations only serve to confirm the teachings of many decades. H. M. Vernon,[28] for instance, in a comprehensive study of the question for the British Central Control Board, in which various dilutions varying from 5 to 40 per cent. solutions were used with impairment of neuromuscular coordination as index, speaks in the same direction. Higher dilutions than 5 per cent. were all found harmful, but the effects of alcohol taken in considerable dilution were found to be much slighter than anticipated. Indeed, he remarks in this connection: "Practically speaking, beer containing 3 per cent. by volume of alcohol or 5.25 per cent. proof spirit is a non-intoxicating liquid."

As to light wines, white or red, the sobriety of districts in France, Italy and Spain in particular, where such are used as usual beverages, speaks in the same direction. This is well illustrated among our own laborers, the best, most orderly and most industrious of which are the winedrinking Italians, as all road contractors will testify. Again, claret is a prophylactic against a class of deficiency diseases now receiving much attention. Suggestive in this connection is the fact, recalled by Bouchardat that claret prevented the development of scurvy aboard a French war-vessel, one of two detained in the South Seas, while the disease developed aboard the other, a British vessel, upon which the usual ration of rum was used. Prof. Bouchardat ascribes the salvation of the French crew to the inorganic matter and particularly the potassium salts contained in their wine. The proportion of alcohol in natural wines varies from 5 to 15 per cent. but the quantity consumed at one time, even of the finer vintages, is far below that of beer, because of their tendency in any large amount, to disturb the stomach, owing to the tannates, ethers, and essential oils they contain. Hence the rarity of intoxication due to wine.

Very different, however, are the percentages of alcohol in whiskey, brandy, gin, rum, etc. (44 to 55 per cent.) which percentages are the real source of all the ills attributed to alcohol as a whole and the use of which it should be our aim to discourage.

*Conclusions.*—All these facts, which could be multiplied almost indefinitely, owing to the vast amount of literature available upon the pharmacology of alcohol, suggest the following deductions:—

1. Alcohol either stimulates, depresses, or causes organic lesions in the endocrines, according to the quantity consumed, and, as such, in keeping with other therapeutic agents, proves beneficial in small or moderate doses, but harmful in large doses, *i.e.* when such exceed, either singly, or cumulatively, certain limits.

2. Pharmacology: Alcohol increases general metabolism: (1) by becoming itself oxidized and thus increasing the heat energy liberated in the blood and tissues; (2) by stimulating the adrenals, which govern the intake of oxygen, and sustain anabolism, and (3) by stimulating the thyroid which sustains catabolism.

3. In stimulating but non-toxic doses alcohol increases the functional activity of the endocrines. This action, through the adrenals and thyroid especially, increases the cardiovascular tone, respiratory activity, the rate of metabolism, and the efficiency of the defensive functions.

4. In toxic doses, the excess of alcohol taken becomes oxidized at the expense of the oxygen in the blood. The tissues, including the endocrines, being inadequately supplied with oxygen, their metabolic rate is slowed, the cardiovascular tone is lowered, and the defensive efficiency of the body is reduced giving rise in marked cases to the symptomatology of acute alcoholism.

5. When the use of toxic doses of alcohol is prolonged, or becomes habitual, the excessive heat energy developed in the tissues by the oxidation of the alcohol increases sufficiently the proteolytic activity of the tissue enzymes to cause autolysis in various highly differentiated tissues including the endocrines, causing therein focal lesions which lead to sclerosis.

6. Therapeutics: Small doses in free dilution are indicated because of their stimulating action upon the adrenals. These organs, by increasing the oxygen intake, add to the heat energy liberated by the oxidation of the alcohol itself, a potent agency for the prompt acceleration of cellular metabolism which entails a correspondingly rapid resumption of depressed vital functions. Hence, the familiar fact that alcohol is indicated in such conditions as circulatory failure including that of acute infections, fainting, shock (all of which conditions, when threatening, may be further counteracted by also giving intramuscular injections of adrenalin), convalescence, senile debility, overstrain, fatigue, etc.

7. General Uses: Beverages containing 3 per cent. by volume of alcohol such as light beers, cider, etc., are nonintoxicating because of the necessity of ingesting too great a volume of fluid to cause any degree of

intoxication. Light wines, white or red, containing 5 per cent. by volume of alcohol are likewise nonintoxicating partly for the same reason, but particularly because any large quantity of wine tends to produce gastric discomfort owing to the tannates, ethers, aldehydes, essential oils, etc., they contain, thus automatically precluding intoxication.

8. The cause of true temperance would be better subserved and a large majority of the antagonists of prohibition would lend it their support for public good, if in its details, the law enforcing it were compatible with the teachings of science and with the needs of the workingman and others in whom fatigue, debility, physical and mental depression, justify the use of nonintoxicating beverages such as light beers, cider, etc., containing not more than 3 per cent. of alcohol by volume, or light wines containing not more than 5 per cent. by volume. The Volstead Act which imposes the rule that one-half of one per cent. of alcohol is intoxicating within the intent of the Prohibition Amendment is not sustained by a single scientific fact, and, as all wrongs invariably do, is steadily defeating its object.

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## ALCOHOL IN SURGERY

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Alcohol possesses a sort of universality which has led it at various times into several fields of surgery. On the whole, we may say there appears to be no place in which it holds a superior position to other agents which may be employed for the purposes for which alcohol is employed.

In advance of the days of ether anesthesia, patients about to undergo surgical operation during the days of the heroic era in surgery were sometimes put profoundly under the influence of alcohol—a resource which is said to be still employed among some of the native tribes in Africa and in remote districts elsewhere, where anesthetics are not available. Alcohol was at one time used in combination with chloroform and ether in what was known as the A. C. E. mixture, which was supposed to lessen the refrigerating action of sulphuric ether and chloroform and at the same time add a certain stimulating influence which would overcome the depressing influence of chloroform. The A. C. E. mixture has, however, now passed out of use for the most part.

In some of the neuralgias alcohol has been used for injection purposes, particularly in trifacial neuralgia, sciatica, and neuralgia of the superior laryngeal nerve occurring in tuberculous laryngitis. Osmic acid, however, in weak solution seems to be more effective and with longer duration of influence than alcohol. Both of these substances are injected directly into the nerve preferably, although sometimes alcohol in the nerve sheath will suffice to halt the severe neuralgic pain. In all probability this action is secondary to a coagulation of albuminous elements in the nerve structure, and the neuralgia is prone to return after a restoration of the nerve elements to normal condition, which naturally occurs spontaneously.

Alcohol as an evaporating lotion diluted with water is a valuable agent for cooling purposes in cases of contusion. Gauze moistened with an alcohol solution and gently fanned produces a very grateful refrigerating effect.

Alcohol has a place in the preparation of surgical instruments. In emergency, other means not being available, certain instruments may be sterilized by "flaming" by means of alcohol. In some operating rooms it is the custom also to boil sharpedged instruments for one to three minutes only and then immerse them in 70 per cent. alcohol. When knives are sterilized by immersion in pure carbolic acid, they are immersed in alcohol before being used. As a general disinfectant of instruments, however, alcohol of ordinary temperatures cannot be

considered to be useful. Various experiments on the part of a number of observers have shown that alcohol is not really a germicide, but it may act as an antiseptic with inhibitory action upon the growth of bacteria. There seems to be evidence that certain bacteria resist the action of 95 per cent. alcohol, that they are not affected by a 50 per cent. solution, and yet 70 per cent. seems to penetrate the bacterial tissue and act as an agent inhibiting bacterial growth. Some species of bacteria, the colon bacillus, for example, are injured more by a very strong solution than by the weaker ones, this matter of response to alcohol varying with different kinds of bacteria.

Alcohol is used extensively as one of the substances for hand preparation and for preparation of the skin of the patient in advance of operation. Its action here, however, belongs to nothing more than that of a general solvent for removing sebaceous material and other materials which hold bacteria upon the surface of the skin. Scrubbing with green soap presumably does more than is done with alcohol in this way, and it has the special advantage of not hardening the epithelium of the hands of the surgeon. Alcohol, being hygroscopic, abstracts a certain amount of water from the superficial epithelium so that a surgeon who employs it several times in the course of a day would lose a certain degree of delicacy of touch that goes with soft skin.

Alcohol in weaker solutions, not stronger than 25 per cent., appears to have been beneficial at the hands of a number of gynecologists for flushing purposes in cases of septic endometritis in connection with a drainage device. The empirical results recorded do not take into account the fact that alcohol is not a germicide, and we apparently have some local stimulating effect upon the normal tissue cells leading them to resist bacterial invasion. The unknown factor may relate to the astringent action of alcohol.

Alcohol has been employed as a preservative for catgut, but it exerts germicidal influence only at boiling temperature and under pressure.

Alcohol as a stimulant after surgical operation, for the purpose of overcoming the effects of shock and for stimulating flagging energies into activity, appears to have a place of considerable importance at times, although a good deal of judgment on the part of the surgeon is required in order to avoid injurious action. Continuous vomiting after surgical operation is sometimes quieted promptly by small doses of champagne, and patients who are making slow recovery from the shock of operation occasionally make prompt response for the better when alcohol is given in the form of good wine or spirits.

In conclusion we may state that alcohol as an antiseptic and anesthetic in surgery has negligible value, and as a stimulant it has limited application.

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## DISCUSSION

Dr. Oliver T. Osborne of New Haven expressed his enjoyment of the papers that had been presented and said that while there was nothing to be added to the scientific end of the discussion he wished to go on record as believing that the medical profession could get along without alcohol in the treatment of disease. That did not mean, however, that there were not indications which were not better met by alcohol than by some other drug. The main point in the discussion of alcohol and the law was the effect on well people. It was a question whether a little alcohol did any harm to a working man after he was through with his labors, but there was no question that alcohol taken in any amount by the individual deteriorated mental and physical work. He did not approve of legislation putting upon the medical profession and the druggists the onus of the distribution of alcohol; and therefore he and many others of the medical profession had taken no license to prescribe it. Many druggists also refused to be under suspicion in the handling of alcohol. It was a serious question as to whether the little alcohol a man might wish as a quieter of his nervous system and for its narcotic effects was not going to be succeeded by getting more active stimulants. There was no question but that the sale of coffee had increased fifty per cent. within the past year, and it was known that more drugs were taken. The harm of home brew and of miserably distilled preparations would soon be in evidence in the form of numerous digestive and nervous ailments. It could not yet be determined as to whether radical legislation was the best way in which to present this matter to the country, but he could not approve of the way it had been put upon us.

Dr. Charles E. de M. Sajous of Philadelphia said that the paper he had submitted was in favor of the prohibition law, owing to the evil effects of the abuse of alcohol. But the Volstead Act was in itself an abuse — an abuse of power in that it imposed upon the public restrictions which were not warranted by scientific investigations which had shown that the three per cent. by volume beverage could not intoxicate. Law-abiding people, whether they approved of the amendment or not, were in entire accord with the proposition that publid morality was not being promoted by keeping on the statute books laws which were creating outlaws on all sides. In most states the people were perilously near the situation of open evasion of the law and fresh technicalities were daily being invoked on both sides to defeat them. Events were increasingly proving that the perverse measures being adopted to enforce the 18th amendment were increasingly nullifying its benefits. In the papers read much had been said about efficiency. There was no doubt that alcohol reduced efficiency; but the point under discussion in the present connection was whether three per cent. beer, cider, etc. or the five per cent. wine taken after work by our Italian laborers, which promoted the hydrolysis of fatigue wastes, was going to do any harm, and whether the fact that we recommended this mild stimulation would not be of distinct benefit and help to eliminate much of the antagonism toward the law. There

was no doubt that if the ugly side of the law were eliminated the good side with all its advantages could be preserved. The influence of the physicians in this matter should not be overlooked. That in nontoxic doses, alcohol promoted the defensive functions of the body had first been shown by Dr. Hare of Jefferson Medical College, and had been repeatedly confirmed in Europe. The profession could do much to preserve the beneficial effects of the 18th Amendment by allowing their opinions to be guided by the teachings of science and opposing the intemperate fanaticism of the Volstead law.

Dr. Spencer L. Dawes of New York said that he had been very much impressed by what Dr. Fiske had said in a statistical way. Of course, anything could be proved by statistics, but he had been particularly interested in the statistical features regarding insanity in the State of New York, showing that it had decreased markedly. The question was, what was alcoholic insanity? There were other features which had to be considered beside alcohol. Dr. Dawes said that he had to deal with all of these 41,000 insane in the State of New York. A man was reported as an habitual drinker—did he therefore have alcoholic insanity? Beside that, would it not have been possible to have had this decrease in alcoholic insanity with an elimination of the hard drinkers? Dr. Gregory talked about the great decrease of alcoholic cases in the psychopathic ward at Bellevue, but he did not say that the number of drug takers had quadrupled. How many of them came in every two or three months? One could not place a great amount of confidence in the statistics regarding the effects of alcohol on the insane in New York State. In the *Medical Record* of May 7, 1921, the following paragraph appeared: *"Alcoholic Cases Increase in Kings County.*— An increase of nearly 120 per cent. in the number of the alcoholic cases in the Kings County Hospital within the last two months has been reported by Dr. Mortimer D. Jones, Medical Superintendent, to Bird S. Coler, Commissioner of the Department of Public Welfare. The report states that 650 persons were admitted to the alcoholic wards during the nine months ending April 1, against 299 for the corresponding period in 1919-1920. The cases have become much more acute in character."

Dr. Jacob Diner of New York said that he recalled very vividly a symposium on alcohol in New York Academy of Medicine before the prohibition act had definitely gone into effect and was still under discussion. Dr. Gregory stated that he antictipated a marked increase in drug addiction as soon as the use of alcohol was prohibited. His prophecy was borne out by the figures mentioned by Dr. Dawes. Dr. Gregory had reversed himself now by reporting the reduced number of alcoholics, but he was careful not to mention the increased number of drug addicts. Dr. Diner said he believed that physicians would rather have a man committed to Bellevue for two to four weeks as an inebriate than to have to deal with a confirmed heroin or cocaine user. There was no question at all but that drug addiction had increased since the ostensible reduction of alcohol consumption.

Dr. Reynolds Webb Wilcox of New York said there was another phase of this matter which this Society as physicians should consider very carefully. Physicians were admitted by the state to the practice of medicine and required in their daily duties to obey three specifications: they should have the proper education, which the Regents of the state took care of; they should exercise due diligence, and they should exercise good judgment. The moment

physicians were limited in the exercise of their professional judgment their usefulness as physicians would undoubtedly be diminished. Dr. Wilcox further said that he had not himself taken out a license to prescribe alcohol; there was no man up or down from the President big enough to make him a saloon keeper. He could conceive that the best educated man and the most conscientious man and the most moral man in the profession might believe that the exercise of good judgment demanded that a patient under certain circumstances should receive much more alcohol than was permitted under the Volstead act. It was easy to conceive a man, with all these great characteristics feeling that there might be occasions in which the administration of other forms of alcohol was needed. The great moral wrong of this act was that it forbade men to exercise the good judgment which the law of the state demanded they should exercise. No moral question could ever be settled until it was settled right, and one was compelled to question the Volstead act and the arbitrary manner in which the regulations were carried out as well as the character of the men chosen to carry them out, men of criminal records who deliberately shot down their fellow men in cold blood without warrant of law. The definition of law was well stated in Professor Robinson's little book, that law was merely crystallized custom. That was all it was. We could not make people good by law, but we could make them bad. Dr. Wilcox said he was told by police magistrates and hospital authorities that men who were now deprived of Wine and Beer were turning to the saloons and drinking whiskey and other liquors of which there was a plentiful supply, thus perpetuating the worst form of intemperance. While he regarded the prohibition act as the greatest economic advance that had ever been made, he also considered that itw as most severely to be criticised and condemned on moral grounds.

Dr. William F. Milroy of Omaha said there were two points to which he wished to call attention in respect to this matter. The first was that probably the great majority of the members of the Society present resided in two or three of the great cities of the country and they should not form their conclusions in respect to this whole question simply from the observation of these few great cities. They must not forget the balance of the hundred million people living outside of these great cities, and the conditions among these people as influenced by this new law. He had heard of people in the State of Kansas, the neighboring State, who had grown up without ever seeing a saloon and some of them had never seen an intoxicated person. They had lived there since Kansas became a prohibition state, and that was the condition in which they had lived to the present time and had lived for years. That suggested the other point, which was that not enough time had elapsed since the introduction of this law for any one to determine finally its ultimate value or consequences. The nation had lived drinking alcoholic liquors of various kinds through all its history, and it could not be expected that in one, two, or even five years it would gracefully submit to the conditions imposed by this law. It was a matter that would take time, and if this present generation of drinkers saw fit to take themselves off by the illegal use of liquors it would leave the country in the future, if this law was carried out with its full intent, a very different country from what it had been in the past; the economic advantages would materialize and the disadvantages would disappear to a very great extent. These two points ought to be recognized whatever might be one's attitude in respect to the physiological or therapeutic value of alcohol.

Dr. Jacob Diner of New York asked whether it was not a matter of fact and statistics that in many socalled prohibition states there was a correspondingly greater consumption of alcoholic "patent" medicines.

Dr. Milroy replied that he could not answer definitely, but that pure food laws of the country would take care of that question in the future as occasion would arise. It was well known that in the formulae of many of these articles the allowance of alcohol had been cut off and restricted. In his own state of Nebraska prohibition had been in operation for about six years, and in his opinion the result had been most beneficial. In his own city with a population of over 200,000 the conditions had improved enormously. Of course it was true that liquor was sold—being imported from Canada and manufactured—but that was diminishing rapidly.

Dr. Eugene L. Fiske of New York said he had tried to make clear in his paper that he drew no positive conclusions from the statistics with regard to the influence of prohibition, but he might have been misunderstood. He had stated that in 1920 the mortality in the industrial population was very low, but he had uttered a caution that no dogmatic conclusion should be drawn from the figures presented from Drs. Kirby and Pollock as regards the effect of prohibition. He made the point that long before prohibition there had been a steady decline in the use of alcohol due to other causes. He had stated that the admissions for drug psychoses had dropped from .38 to .28. He thought he had not read some figures relating to the proportion of users of alcohol in various groups investigated. It was generally considered that total abstainers formed a small minority of the population, that they were a peculiar group. The New England Mutual Life Insurance Company, through its investigations extending over 60 years, showed 38 per cent. of practically total abstainers. In two other companies including one containing many Germans, the proportion was 64 per cent.; in another 56 per cent.; in other industrial groups, 45 per cent.; commercial groups, 72 per cent.; and to these might be added a number who used alcohol casually but were not committed to its use. From what he had observed by intensive study of all the facts, he could see very good reason for figuring out a majority against alcohol, and it was erroneous to form the opinion that, because a great noise had been made, a group of agitators had put this thing over. Personally he had never engaged in anti-alcohol propaganda, but had collected facts and let them be used for what they were worth. He did not offer his paper as a brief for prohibition, but he did believe prohibition had been a wholesome thing. He believed that the forces of education and the practical common sense of the people were for a reduction in the use of alcohol before the law decreased consumption, and was inclined to agree with Dr. Kirby that there had been growing up a sentiment against alcohol and that political agitation had not had a great influence in the matter.

Dr. John C. Hemmeter, in closing said that the blood of the human being normally contained under physiological conditions 3/1000 proportion of alcohol. The blood of several total abstainers examined, who lived largely on carbohydrates contained a slightly higher proportion of alcohol. The distillate of the human feces yielded a considerable percentage of alcohol, being largely from intestinal fermentation of carbohydrates and sugars, for the alcohol was made from the sugar; and as total abstainers were proverbially large consumers of sugar they distilled a little more alcohol than the consumer of alcohol, for the

latter lived largely on a protein diet, from which no alcohol could be formed. It would be interesting to watch this situation, for the total abstainer would be the unconscious manufacturer of alcohol since he had the most favorable conditions for forming it. That little moonshine distillery was working all the time, and though the percentage of $C_2H_6O$ formed was small, yet it could only be estimated as having a pharmacologic effect because of continuous action; whereas the man who took his regular drink used it sporadically. Experiments on the isolated dog heart reported in the English *Journal of Physiology* eight years ago brought out the fact that when measured amounts of Ringer's solution mixed with different percents of alcohol were profused through the heart and circulated through the coronary arteries, the blood oxidized the alcohol and those animal hearts performed a greater amount of work than the controls without alcohol. This was mentioned as being of biological interest at any rate.

**Alcohol Is of Therapeutic Value.**—Dr. Lewis H. Taylor of Washington said that the Council of the American Therapeutic Society had instructed him to present to the society the following resolution: *Whereas* the use of ethyl alcohol and its preparations is not only justified but also indicated by observations made by laboratory investigators and clincal experience, therefore be it *Resolved by* the members of the American Therapeutic Society in convention assembled that alcohol has a proper place in the treatment of disease; and be it further *Resolved* that the least possible restrictions in the use of the drug compatible with the enforcement of the 18th Amendment be imposed on the members of the medical profession; and be it further *Resolved* that a copy of this resolution be sent to the proper authorities.

Dr. Oliver T. Osborne of New Haven said that he was not opposed to the resolution but at the same time he was not sure he wanted the American Therapeutic Society to go on with a rush. They should be deliberate in a resolution which was likely to be misunderstood and misinterpreted. He did not see that there was any way our methods of giving or not giving alcohol could be helped by the resolution. He did not wish to be on record as opposing the Volstead law if it was modified into a decent law. He did not approve of the law as it stood.

Dr. Jacob Diner said that Dr. Osborne was losing sight of the fact that the enforcement officers had the power to make whatever rulings they desired in order to stop the use of alcohol. That might lead and probably would lead to an entire upset of all pharmacopeial preparations. The prohibition officers had already promulgated certain changes in the U. S. Pharmacopoeia preparations. Unless we took a definite stand and recognized the necessity of the use of alcohol in some form or other as a drug it might not be so very long before no tinctures or elixirs could be prepared, because thay all contained alcohol. It might mean the abrogation of our privilges to prescribe a drug to meet certain conditions. This resolution was not in favor of antiprohibition but merely for the protection of the right of the physician to use drugs as deemed necessary in the treatment of disease.

Dr. George H. Hoxie of Kansas City supported Dr. Osborne in his contention, for he believed that as medical men they would make a mistake if the society mixed in this fight. It seemed to him that the best attitude for medical men to pursue was the scientific one, keeping away from any discussions that would belittle them or tend to put them on a level with saloon keepers. He

had himself refused to take out a license to prescribe alcoholic drinks. He agreed with Dr. Wilcox that the society should abstain from anything that might appear like coming down into the plane of the antiprohibition fight. He himself happened to have lived in Kansas, having been a member of the faculty of the State University for several years, and he could testify somewhat in answer to the question that had been put by Dr. Diner. He had found it a very delightful place to live in, and had found no difficulty whatever in prescribing whatever drugs he needed, and he did not believe the people of the state were to any extent damaged by prohibition. For the last few years he had lived in Missouri which had been wet until the Volstead act and could therefore contrast the wet with the dry neighborhood. If he had a choice of location without knowing anything more about it than one was wet and the other dry, he would select the dry state. He did not believe the medical profession had been or would be interfered with in any legitimate way. If a protest as to the present condition of affairs was needed it should be made by those injured and not by the doctors. If the patients really did suffer their protests would reach Congress more effectively than if this society, a small group of medical men, should enter such a protest. The majority of the men present were from the East and it would be wise for them to heed the warnings of Dr. Milroy and himself who represented another section of the country, and one that was vitally interested in the matter.

Dr. Reynold Webb Wilcox of New York suggested that perhaps Dr. Osborne should bear in mind the fact that the trouble caused to physicians resulted not so much from the enforcement of the various acts of Congress and amendments to State laws—not from the laws themselves, as from the interpretations which had been put upon these laws, the rulings that had been made. In those cases that had had to be defended in court in order that the rights of human beings should be protected, it became necessary to point out to the court that the burden of proving that these rulings were germane to the law rested upon the district attorney, and that if they were germane to medicine and not to the practice of law they were rulings that the commissioners and the district attorneys would attempt to force at their peril. That was the law. He would dislike very much to have the society leave the matter as it stood at the present time, because if they should fail to act now the Associated Press would send out the news that the American Therapeutic Society declined to take action upon the value of alcohol as a therapeutic agent when that decision was to be based upon scientific grounds. That he would regard as very unfortunate. Personally he would like to see the very carefully drawn resolution passed upon by a large majority, and should it be so passed action by any other medical society would be entirely superfluous, because this organization, representing the best and most scientific knowledge as to the medicinal use of alcohol, would render a decision which could not be even questioned.

Dr. J. Madrim Taylor of Philadelphia said he had heard a sudden resolution presented and was asked to vote for it; but he wished to make some pertinent response. This question could not be passed upon by this or any other body unless it contained a certain number of competent psychologists. It was the question of the effect of alcohol on the average individual. He did not believe this matter had been taken into proper consideration, and he objected. That was his stand.

The Society then voted upon the Resolution and it was adopted by a two-thirds majority.

# ON THE PREVENTION OF VENEREAL INFECTION

By THOMAS E. SATTERTHWAITE, M.D.,
New York

Last summer I called the attention of medical practitioners to the great increase of late in the ratio of infection from venereal diseases among the British, our own military forces in Europe, and also the Canadians, contemporaneously with the recent war activities. I also called attention to the fact as mentioned by Dr. Joseph E. Moore, one of our military officers stationed in Paris, that at one time 70,000 prostitutes plied their trade there unmolested by the police. I also stated, on the authority of Morel, formerly a member of the English parliament, that wholesale infection of girls and women, in the occupied enemy zone, was caused by some of the French colored troops. This matter found its way at various times into the public prints and led to public discussion which resulted, after a time, in amelioration of these conditions, if we are to accept newspaper reports. Further, in an article published last autumn I stated that the incidence of venereal disease in Paris at the time above mentioned, was, according to Moore, about 330 per thousand, among our troops there, or about one in three, while among the British troops, there at the same time, the incidence was said to be about 200 per thousand. Now assuming that the British rate among their military in time of peace was about 50 per thousand, a pretty fair estimate, I think it is quite evident that venereal disease in Paris had at that time assumed the character of an epidemic.

But more than this, we have been told by Sir Archibald Reid, in his "Prevention of Venereal Diseases," 1920, that "nearly all the troops from France and Germany which came to him in the early part of the war were infected (p. 133), while after the American troops landed in France, 104 infections out of 100 were noted in some units (p. 272). In occasional instances, of course, two or more infections at different times, in the same individual made this otherwise impossible ratio possible. Moreover, he stated that so far as Great Britain was concerned, when he was writing his book, something like every other person in the United Kingdom had suffered or was suffering from venereal disease (p. 329). This statement is, one would think, too broad for acceptance. At any rate, I believe the loss to a nation from these diseases in health, in happiness, and in efficiency far transcends the loss from any other source, even tuberculosis, which was once held to be the most fatal scourge of the world.

But when we come to think that syphilis and gonorrhea, or at least the affections to which they may give rise, are apt to be incurable,

their dangers become more apparent. Indeed, we must not forget that gonococcus infection, once thought to be a comparatively mild affair, may actually effect directly or indirectly disease in any part of the body in either sex.

That these manifestations may also be incurable or lead to fatal results, will be admitted at the present day by medical practitioners generally. Gowers once said of syphilis, and his name should carry great weight with us, "it is an incurable disease. No treatment," says he, "however thorough, will bring syphilis as a disease to an end. Syphilis," he also added tersely, "is unrivaled in its total capacity for wrecking human happiness and health and life by any other disease." As to prevalence of syphilis in these latter days, Riddell, a Canadian government official, has told us that in 1920 there were more than half a million syphilitics in Canada, and 40,000 in Toronto. How large a percentage of the belligerent troops were infected is a matter as yet indeterminate. I have thus far seen no satisfactory statistics on the matter, nor have our own statistics impressed me as to their accuracy.

But Miss Ettie A. Rout (now Mrs. Hornbrook) has stated that probably no European country had less (in 1920) than three or four more times the amount of venereal disease it had in 1913 or 1914. Incidentally, I may say it is my impression that the colored races were largely responsible for its recent dissemination. In some parts of Africa, such as Egypt, or territory adjacent to it, such as Madagascar, the incidence is, I am inclined to think, greater than in any other part of the world. It is endemic in some of these places. Reid has charged his own nation with being most active in spreading it. But I think, he may not distinguish the native Anglo-Saxon from the Colonial. The degree of infection in some colored races was alluded to in a recent public discussion that took place in England, when Viscount Knutsford told of a call of two vessels at a West India island, where he said venereal disease was "frightfully prevalent." On one ship with 650 aboard, 160 cases of syphilis were found after the vessel had left the port, the inference being that the disease had been contracted in this particular island.

Since my article appeared Miss Rout has written commenting on my opposition to the so-called "preventive treatment," stating that as the result of it between Nov. 8, 1917, and March 30, 1918, the ratio of infection was reduced from over 20 per cent. to less than 3 per cent. She stated also that the licensed houses in Paris, "made the least dangerous provisions for the normal sexual needs of the men," and that they were "infinitely preferable to the unlicensed house system of London." She said in fact, "This French system, supplemented by our

own issue of portable disinfectants to Anzac soldiers (Australians and New Zealanders), and aided by the American Red Cross Dispensaries and the American Army Prophylactic Stations (all of which made our soldiers welcome to their medical benefits), was responsible for the fact that Paris gave us the lowest rate of infection in 1918, whereas London gave us the highest." There was evidently great danger outside of these French houses, for he says she found that in one haul by the French police, of 100 prostitutes, 91 per cent. were infected with venereal disease. In a foot-note, however, we are naively told by Miss Rout not to put too much confidence in the figures given as to the ratio of infection in Paris, for one of the officers at the Red Cross Conference in April, 1918, said he believed a number of officers were not reporting themselves, and that in other ranks the ratio of incidence should be doubled. One reason for the lack of value in these statistics was stated to be that, after the armistice at least, it was feared infected persons might be detained during demoblization. Apparently to some exent these diseases were concealed. One must note that the friendly aid of our American Red Cross Dispensaries and American Army Prophylactic Stations to their co-belligerents was duly appreciated by Miss Rout.

According to our Surgeon General's report we are told by Miss Rout also, that "During the fifty-three weeks ending September, 1918, there have been 178,204 venereal disease cases reported under treatment in the United States Army in France. But the reports indicated that approximately eighty-five per cent. of this number entered the army already infected, that approximately only fifteen per cent. of all cases reported were contracted after enlistment." From which we must draw the obvious conclusion that our examining officers admitted to active service infected men, and in very large numbers. This would naturally, if true, shift the onus of permitting infection from the officers in the field and throw it back on the enlisting officers. It is, I think, an established fact that incidental to departure, men going into active service were often examined very superficially. In fact Miss Rout maintains that of 44,167 cases of infection in France among our men, 96 per cent. were contracted prior to their entering the service. If this be true, we evidently have to accept some of our official statistics with grains of salt.

Of course, where these venereal diseases were contracted and who is to blame for the infections will probably never be determined in a satisfactory manner for obvious reasons. And yet these diseases that are being spread all over the world bringing affliction, misery, and even death into hundreds of thousands, perhaps millions, of our families, could in the great majority of instances have been prevented. For

usually they were produced by immoral practices that could have been avoided. The accidental examples of infection represent only a very small percentage of the whole.

But what has been done in the way of prevention during these fateful years? The action of the British Royal Commission of 1916 is an example of what was suggested by one association in the way of prophylaxis. It passed a series of recommendations, such as that greater opportunities should be given for treatment of the infected; medical men and students should be afforded better chances to study the diseases; there should be better cooperation between associations undertaking to care for the infected; and courses of lectures should be given showing the dangers of infection. This might be called the Soci-educational Plan. The main issue was avoided. In fact it has been alleged that the incidence of infection increased under the plan. It probably was so. The disinfectant method, however, was largely recommended and to some extent put in practice by men such as Sir Archibald Reid and others. It was recommended by the British Society for the Prevention of Venereal Disease, though opposed by the British National Council for Combating Venereal Disease. Various disinfectants were used, such as calomel in oinment form, solutions of the bichloride of mercury and of protargol, and permanganate of potash, also green soap. The disinfectants were put in vials or collapsible tubes. Also there were furnished pledgets of absorbent cotton, syringes, nail brushes, and towels. These comprised the contents of the prophylactic packets made extensively for the use of the soldiers. This method might be called the Prophylactic or Direct Method. Unfortunately for its efficiency the outfits were often used after, not before exposure. After the horse had been stolen the stable door was locked. But the men were willing to take the chances. Women of the prostitute class, however, the most dangerous seldom, it has been said, would take prophylactic treatment, and for various reasons. Sometimes they did not realize they were infected; perhaps they were unwilling to take the time for disinfection; or perhaps thy knew that effectual disinfection was very difficult and not always possible even by experts. In this connection it may be said that the examination of public women as practised abroad, has sometimes been so improperly done that noninfected women have been infected, the reckless carelessness or indifference of the examiners actually carrying the disease sometimes from one to the other. Even in New York City our Venereal Disease clinics have not been what they should be as to cleanliness and other requisities. We have among us now a class of individuals, and it is not small, who look with indulgence on promiscuous intercourse, at least in so far as that they advocate

chiefly methods in which disinfection before or after exposure is the cardinal point. This plan is practised in both our military and naval forces and those of great Britain, though in the case of the latter it has met with considerable opposition, notably in clerical and legislative circles.

The other side of this question was ably seconded during his life by Sir James Paget, who said in an article on sex hypochondriasis (p. 286), "Chastity does no harm to mind or body," and Paget's influence in his day in medical circles was second to none. Sir George M. Humphry, the famous anatomist and surgeon of Cambridge, England, has also stated that the functions of the testicle "may be suspended for a long period, possibly for life, and yet they may be sound and capable of being roused into activity," (p. 151) and Sir Thomas Bryant in quoting this clause adds (p. 754) speaking of the testicle that "unlike other glands, it does not waste or atrophy for want of use."

I had the pleasure of knowing these three gentlemen personally and they represent to me examples of the highest type of our profession.

Also the famous neurologist, W. R. Gowers, previously alluded to, has said "One method and one alone is possible in man, and that one is open to all. It is the certain prevention secured by unbroken chastity" (p 126).

Max Hubner, one of the latest of the contributors to this subject, has confirmed this view, stating he has seen no harm in continence, but rather that it is one of the keys to a solution of the problem (p. 261). Herein is the truth. It is a key and at present the best key at hand. But there are others. One is quarantine. It was my privilege once, while in military service abroad in France, to be put in sanitary control of a small town, within the area of hostilities. The officers and men were becoming infected in increasing numbers. I was given the requisite authority and had the public prostitutes sequestrated. As a result there was a prompt abatement in venereal diseases among the military. In fact no new cases came to my notice. This incident I have alluded to already in a previous article. Such a method may be successful in military circles but cannot well be applied in civil life under our present laws in this country. But there is already a new move in the proper direction in this respect. Recently a District Court of Appeal in California upheld the right of a local health officer to detain and quarantine persons having a venereal disease.

Such legal action is not an infringement on the liberty of the individual any more than the quarantining for other infectious diseases.

In the face of impending danger to society, the individual should yield his individual rights. It is done in tuberculosis and in various other diseases and the same rule should apply in venereal diseases, which, as I have said, are much more dangerous to our life and well-being.

But there is a third method. It is also a legal way. Take the Swedish venereal disease law, which went into effect Jan. 1, 1919. It provided in effect that: (1) every person with venereal disease was to be treated appropriately and so prevented from infecting others; (2) the source of the contagion was to be sought and suppressed, and (3) penalties were to be imposed for exposing others to contagion. In these matters, all were made to stand equal before the law. Individual rights must be subordinated to collective welfare. At first the returns from this Lex Veneris showed hardly any reduction from preceding figures, but against 3,355 cases at the end of 1919 there was a drop to 2,495 in 1920 in one locality. In Denmark, also, there has been a move for betterment. If, for example, a citizen should undertake now to keep a public brothel or rent rooms for immoral purposes he would be liable to a prison sentence. In our own country, too, the Supreme Court of North Carolina has approved a judgment in favor of a wife who has asked for punitive damages because her husband infected her. Since then two other State courts have held that the wife has a right to recover damages for injuries to her, as in the case just cited.

It can hardly, therefore, require much vision to see that woman, being no longer a chattel, may demand protection by the State against conjugal infection and that this needed protection will be afforded her eventually by the country at large. But it is the fashion of the day, as I have said, to advise other methods. And yet I do not believe that much has been accomplished by such efforts as have been made in the way of prevention by the United States Public Health Service, boards of health, and private or semiprivate associations to combat venereal diseases through the instrumentality of public lectures, posters, and publicity in general. These methods have some value, I admit. Some of them emphasize, however, a popular fallacy that prophylaxis can effectively *prevent*. Even the friends of disinfection do not seem to realize that it is effective so far as we can learn in only about two-thirds of the instances where it is employed. Assuming, as we may, that disinfectants kill the gonococcus and the spirochete in vacuo, this is a very different affair from destroying the germ in the living person. Miss Rout, indeed, has told us, and one may well believe it, that "wherever prophylaxis was properly applied, at least two-thirds of the cases of venereal disease were eliminated." But what about the one-third of failures?

Now with the exception of accidental cases, chastity and the strong hand of law do offer chances that we may eventually master this worst of all international plagues now threatening the whole civilized world, just as Europe was threatened by syphilis, the "great pox" of the middle ages.

Disinfection undoubtedly has its place as a precaution against contagion, and as a curative measure, but it should always be remembered that the so-called prophylactic methods protect to a limited extent only.

Also it should be realized that limitations of the danger do not tend to discourage improper relations with their attendant dangers. In fact, they encourage it. Infection is always possible and probable so long as promiscuous intercourse is practised with women, whether prostitutes or others.

7 East Eightieth Street.

## DISCUSSION

Dr James M. Anders of Philadelphia said that prophylaxis in venereal disease was essentially a medical question and that from the medical profession must emanate efforts to solve the vexed problem. This being unquestionably true, they should realize their responsibilities, more particularly since, as Dr. Satterthwaite had just emphasized, these diseases had been more prevalent since the World War than prior to 1914. It had been thought that the prevention of veneral disease could be dealt with by Boards of Health, *e. g.*, by making notification compulsory, etc., but it had been shown in Philadelphia and elsewhere that notification was not practicable and could not be enforced at present. He had been a member of the Board of Health for eight years. Three years ago the veneral diseases were placed on the list of notifiable complaints, but it soon became apparent that neither the public nor the physicians, more particularly the urologists, were in sympathy with the plan and therefore it was almost totally disregarded. There was, however, a small class of cases to which Dr. Satterthwaite had incidentally referred, in which this regulation had worked well, namely, the class composed of those who were refractory and would not remain under treatment until cured. These cases were reported to the chief medical inspector, Dr. Cairns, who insisted that they either return to their medical adviser or be sent to an institution. This was good so far as it went, but it did not meet the main problem of venereal disease prevention. As Dr. Satterthwaite had initimated, public prostitution was the greatest danger and it had to be controlled by law enforced by the military and civic authorities. The medical profession, however, had a clear and patriotic duty to perform and the same was true of medical bodies such as the American Therapeutic Society, for they should instruct not only the public but military and civic authorities in this class of complaints and how best to accomplish their prophylaxis. The general public was not sufficiently informed in regard to the prevalence and the grave, far-reaching dangers of these loathsome affections, and this information should be spread not only by the medical profession but by military officials and the boards of health. The latter had been carrying on a pretty active propaganda along this line, but unfortunately this reached mostly the medical profession. Dr. Anders said he strongly favored the teaching of sex hygiene in the schools and colleges, and this instruction should include emphasis on chastity upon which Dr.

Satterthwaite had insisted. The general public should be impressed with the fact that chastity is not hurtful to either man or woman. That was an aspect of the subject which had been sadly neglected in the past. Men very often exposed themselves to risk through ignorance, and it would seem that the medical profession was somewhat at fault in not having sufficiently emphasized the importance of chastity among young unmarried men. He felt that as individuals and as an organization it was their duty to speak frankly to the public and inform them of these facts and of the great prevalence and far-reaching dangers to life in connection with venereal infection. As Dr. Satterthwaite had said, there was in London a society for the prevention of venereal disease. That society did not attach much influence to moral suasion, but it did insist that all who would persist in exposing themselves to risk should purchase, carry, and use a simple disinfectant which had been found to be efficient in warding off venereal infection. There could be but one opinion on that point, namely, that the advocacy of such methods must encourage rather than diminish prostitution. Dr. Satterthwaite had dealt with the subject in a very masterful fashion and the paper deserved to be widely circulated and appreciated.

Dr. Spencer L. Dawes of New York said that Dr. Satterthwaite's presentation of the great dangers in public prostitution and also of the prevalence of venereal disease among aliens had impressed him very forcibly, and it might interest the society to hear a statement regarding these two points as related to the hospitals for the insane in the state of New York. It was a very remarkable fact that the greatest ratio of general paresis in the state hospitals in New York today was found among the Italians, and greater among women than among men. That was a very appalling and dreadful statement to make, but in a way it could be explained. There had never been a record anywhere of such a rapid syphilization of a race as among the Italians coming to this country, and it was because of the fact that so many of the Italian men came to this country alone, without their wives and without their sweethearts; they stayed for a time and were exposed to public prostitution, and contracted syphilis, and then later sent for their wives and sweethearts and conveyed the disease to them, and in that way we had the spread of the disease, the incubus falling upon the Italian women.

Dr. Jacob Diner of New York said that the subject presented by Dr. Satterthwaite was of equal importance to that of alcohol, if not greater, and he thoroughly agreed with Dr. Satterthwaite and Dr. Anders that it was primarily a matter of education. He desired, however, to emphasize the fact that education should be spread in a broader way even than through the physician, though his influence was necessarily great. We were living in an era of readjustment, in an era of strife for the single standard. He thoroughly approved of the single standard, but not in the sense in which that was being taken today, of the low standard of the male, but rather of the high standard previously held for the female. Our progressive women of today demanded equal rights with the male. He would prefer to see the restrictions applied to men as they had been applied to women in the matter of sex relations. When a young woman of today selected her life partner, it was not a question of what his previous moral life had been nor what his present physical condition was, but whether he would be able to support her in the style she had been accustomed to at home; that seemed to be the only determining factor in the eligibility of the man. The idea might seem utopian, but he believed that the eligibility of the male should be the same as that of the female, in the chastity and purity and moral character which he brought into the home.

Dr. Beverley R. Tucker of Richmond, Va., said that he had been asked by Dr. Satterthwaite to discuss the paper, and expressed his accord with the remarks of Dr. Anders. He felt that chastity was an ideal which would not be reached in the present generation although it should be the goal aimed for, but we had to get down to something more concrete and practical if we proposed in any way to solve or help solve the question today. In Richmond they have had very efficient city health regulations, and venereal diseases were reportable by name or number; the physicians could keep the names confidental. Those infected had to stay under treatment until three negative smears were made in gonorrheal cases or until two negative Wassermann tests were made in syphilis. The physicians had responded very satisfactorily to this plan, and the cases which did not return to the physicians were taken up by the city and treated at the public clinic or in the city hospital under restrictions, or in the city jail under arrest. In that way the majority of the cases had been gotten under control. An infected man was asked to tell where he got his infection, if he could. If he did not know, he was excusable, but most of them would tell. Sometimes several men would report on the same female, and then she was located and taken in charge. Of course the plan did not work perfectly, but it had lessened very greatly the prevalence of venereal disease in Richmond, where a third of the population were negroes who were very hard to manage under this regime, for very few of them went to a physician. They did not seem to have the disease in a very virulent form, either in the early stages or in the late nerve manifestations.

Dr. John Travers of Baltimore said that the admirable paper of Dr. Satterthwaite was well worth remembering. As a ship surgeon during the war, his own records bore out the statements that had been made. He had been on a U. S. transport taking the troops over and bringing them back, and the percentage of cases of venereal disease in the beginning of the service was over 40 per cent. Whenever they stopped at St. Nazaire or other port abroad, on the return trip, the percentage increased, even among the crew, to 75 or 78. On the last trip, after the armistice was signed, a lot of engineers was brought back and the percentage was something like 92 per cent.

Dr. Hyman I. Goldstein of Camden, N. J., said that if the plan of reporting these cases was adopted, complete reports should be made. If they were going to be used for statistical or other purposes the job should be done completely or not at all. Various laws had been prepared and passed for more or less indirect methods of reporting venereal disease, and in many instances they had proved to be more or less of a failure. To illustrate concretely what he meant, stated that several years ago in the state of New Jersey a bill was passed making syphilis and gonorrhea reportable diseases, to be reported in full—name, address, place of occupation, and if possible the source of the infection. Not long after the passage of this bill he went into an ice cream saloon, and serving the customers was a man with typical secondary lesions on his face, a mucous patch in the mouth and angle of the lips, and lesions on the hands. Dr. Goldstein said he asked the man if he was under treatment and whether he knew that he had a contagious disease, and advised him to see a physician. He then reported the case to the State Department of Health as he was required to do under the law, but nothing further was done. It was impossible to say how many cases of venereal disease that a single patient caused. In another instance, a married man

(early marriage did not necessarily prevent the spread of disease and it was principally an economic question) who gave a history of having had a sore throat for two months, and some pain in the chest. He was told to strip, which he very reluctantly and hesitatingly did. He was a well-known business man and had a family of five or six children. However, he stripped to the waist, and on assuming a certain position a faint macular rash was noted under the surface of the skin. With considerable hesitation the man then permitted a further examination and an active initial (genital) lesion was found. Upon being asked how long this had existed, he replied for six or seven weeks, and that he was under the care of two physicians. Dr. Goldstein said that his object in speaking of this case was to show that it was sometimes a question for the physician himself. There was little doubt but that this man had infected some member of his family and the physicians were directly responsible. The Wassermann blood tests were strongly positive, of course. The dark field examination and Blood Wassermann tests were not made by the previous medical attendants. The matter, however, narrowed itself down to the practical question of how to handle the subject now. The ideal way, as outlined by the speaker, was certainly the preferable way, but this would take time. His own opinion was that a physician was not opposing the prevention of venereal disease by recommending prophylactic treatment to patients who would not follow out the ideal instructions. He also felt that the reporting of these cases, as was done in New Jersey, was a good thing, but that it should be done thoroughly by all physicians and hospitals. It was a very important economic question. When the necessities of life became cheaper and living conditions were changed and readjusted, the young people might mate sooner, and this would tend to reduce the number of infections, but the main point now was for the doctors to make prompt, careful, and early diagnoses, to advise strongly against extramarital and illicit exposure, and where necessary, to give the information pertaining to prophylactic treatment as has been recommended and carried out in the United States Army and Navy.

Dr. Satterthwaite said, in closing, that mistakes were often made in the diagnosis of syphilis. One of the members present, had a case of aortic disease which he had seen with him in consultation. The possibility of its causation being due to syphilis had not been broached. Later Wassermann tests proved that lues existed. Another of the members had transferred to him for a cardiac lesion, an old lady, a spinster, and well connected. On admission to the hospital a diagnosis of tertiary syphilis was made immediately, by the examining physician. In the rural districts of this country, especially, syphilis was apt to be overlooked by the general practitioner, who often had seen so little of the disease that he did not know its phases. Syphilis existed, he could safely say, in at least one-tenth of our population. In cities and congested localities, the incidence was very much greater, of course. As for the efficacy of quarantine in the matter of public prostitution in military circles, he read a cutting from the *New York Medical Journal* of the fortnight previous, in which a statement was made that under the direction of our Surgeon General, it was tried in a group of about 12,000 men, and following it the incidence was reduced about 50 per cent. This incident confirmed what he had said in his paper, that quarantine in military circles could accomplish a great deal. But what we had to do in the future was to protect both men and women by law. If a man or woman contracted the disease and communicated it to his or her consort, it should be a legal matter. We would

probably come to that very soon. He would add a few words about the poor prostitutes. The general idea was that they were purely mercenary women. As a matter of fact, however, there had been many cases, especially abroad, since the war, where women had been forced into prostitution from hunger or destitution. Another point he would make was that these women were not always treated properly in civil life. It had been intimated in print that public venereal clinics were sometimes conducted in so careless and slovenly a manner, as to suggest that healthy persons, especially women, who happened to be suspected of venereal infection, might actually become infected in the clinics.

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## SOME PRACTICAL OBSERVATIONS ON ENDOCRINE THERAPY

By J. M. ANDERS, M.D., LL.D.,
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It may be premised that a summary of the more practical phases of endocrine therapy is much needed by the present-day clinician. That the subject occupies a commanding position at present no one will deny; but it is equally true and of signal importance to recollect, that some of the claims advanced by certain writers for hormonopoietic products are not supported by undoubted facts. Apparent advances in certain directions have too often proven to be kaleidoscopic. The chief weakness of glandular therapy has lain in our inability to discover and interpret the functional interrelations of the various endocrine organs.

With the progress, which we owe to the labors of Sajous, Ord, Kendall, Janney, Osborne, Goetch and others, of exact knowledge of the subject, the limits of usefulness of animal extracts are gradually being settled; and the time has arrived when a broad line needs to be drawn between those endoctrine remedies which are practicably worthless in certain conditions at least, for which they have been vaunted, and those that are worthy of general employment to meet certain, definite indications. This can be done only by subjecting each glandular preparation and its uses to critical analysis, interpreted in the light of experience and experimental invstigation. Pure empiricism in the use of animal extracts, be it remembered, is incompatible with medical standards of progress in therapeutics. Again, individual experience is, as a rule, too small to base thereon reliable inferences as to their value.

Disregarding the centuries spent in unprofitable speculation and fruitless investigation foreign to the purpose of this presentation, attention will be directed only to the more recent acquisitions to our knowledge of opotherapy and its application to the treatment of disease. It is regrettable

that firms manufacturing these products issue pamphlets which purport to give the scientific investigations on which the claims set forth with respect of the extracts are based. Whilst this historic information may be accurate, in some cases, it needs to be verified by reference to scientific literature in all, before it is accepted as authentic and complete. True it is, however, that certain firms will be found to publish reliable information in every detail.

In addition to the clear clinical indications for the use of glandular extracts we must also concern ourselves with their supplementary effects. Moreover, we must not be unmindful of minor degrees or earlier stages of dysfunction, when it is difficult in the extreme to recognize any of the features which ordinarily make up the characteristic syndrames. These, however, call for and are readily amenable to appropriate specific organotherapy. In this connection the fact that primary hyper- or hypofunction of a ductless gland will in its course alter the functional activity of others is to be stressed, so that indications may be presented at times for the use of multiple extracts. Poly glandular preparations, however, must not be resorted to until clear and convincing evidence that more than one of the several glands are deranged as to function. It is always worth while to attempt to identify the gland solely or principally at fault, and to make trial of a single extract at first, if the promotion of our knowledge of glandular syndromes and their treatment is, as it obviously should be, desired. An accurate diagnosis by exclusion of the primary involvement of a single gland, therefore, must precede successful endocrine therapy whenever practicable. Cases, however, are met with in which a diagnosis can be made only tentatively. In such, the cautious employment of corresponding glandular extracts which are to be advised may serve to confirm the diagnosis.

In no case, however, of a mild or ill defined form of glandular dysfunction should these agents be resorted to after a superficial examination, but only in those in which a close scrutiny of the history, clinical data, and laboratory aids has been made and carefully weighed. Lawrence[1] has emphasized the value of a careful history which gives more valuable evidence in the earlier stages of any disease than all other methods of examination. He well says "Physical examination will exclude organic disease, and laboratory tests are extremely useful in determining the degree of abnormal function, but the history, if the symptoms are properly elicited and valued, not only discloses the nature of the derangement present, but gives a measure of its effect upon the patient. If properly analyzed, the evidence it affords is not indefinite, but affords, especially in the case of the internal secretions, a definite basis for differential diagnosis."

It is particularly important to note the basal metabolic rate in suspected thyroid or pituitary involvement. For example, there is no better criterion

of slight though positive deviations from the normal either toward hyperfunction on the one hand or hypofunction on the other of the thyroid gland than the rate of metabolism. This, then should serve as a guide to endocrine therapy, if the history and symptoms presented are confirmatory. A complete diagnosis embraces the stage of dysfunction encountered in the individual case. In treating cases af glandular derangement, the clinician must also meet the hygienic and therapeutic indications of the predisposing factors as well as any associated diseases in the given case. The writer has learned from personal experience to appreciate the fact that the beneficial effects of the class of products under discussion are more limited than certain enthusiasts would have us believe.

If the sufferer be the subject of disease of the heart or kidneys, preparations of the thyroid and pituitary glands are not without danger and may be fatal. The writer recalls a patient with advanced myxedema and associated mitral regurgation, which occurred at a time when a cautious increase of dosage was not generally observed, and a maximum of 5 grains t.i.d. suddenly proved fatal. We know too little about the subject of endocrine diseases and their etiology and associated pathological states to warrant the indiscriminate, not to speak of the reckless, use of animal extracts.

Again, the clinician has to deal with the so-called "ductless gland neuroses." Hemmeter,[2] Friedman,[3] and other writers have, with justice, claimed that all ductless gland disturbances may manifest themselves clinically without macro- or microscopical alteration of these structures. W. Langdon Brown[4] discusses the relationship of the sympathetic nervous system to the endocrine glands and strongly emphasizes the interdependence of the latter and the vegetative nervous system. In this connection the following quotation from his paper is of special interest: "Designed as an intensive preparation for action or defense, the sympathetic response may be so dissociated, perverted, or prolonged as to produce through the thyroid gland Graves' disease with its danger to life, through the pituitary body, diabetes insipidus with its attendant discomforts, through the pancreas and other endocrine glands, excessive mobilization of the blood-sugar, which is the first stage of the metabolic disorder that culminates in diabetes; it may disorganize digestion by exciting spasm and atony in stomach and bowels, and inhibiting the secretion of digestive juices; it may keep blood pressure at a level which is inappropriate for the task of the heart and the arteries. These effects are not necessarily distinct—thus, intestinal stasis from sympathetic inhibition causes poisons of putrefactive origin to be absorbed, which in their turn lead to vasoconstriction and hence an unduly raised blood-pressure." Obviously, a knowledge of visceral neurology is essential to the successful management of diseases of endocrine origin.

Langley and Elliot claim that epinephrin in all its actions on any organ

behaves the same as electric stimulation of the afferent sympathetic fibres of that organ. Moreover, it is well understood that if the organ extracts contain any protein, there is an added protein therapy effect. There is much evidence available to show that both suprarenal and pituitary extracts increase the immune reactions, as shown by their effects upon the agglutinins in typhoid and other fevers. Again, in this power to promote the functional capacity we have an explanation of the hemostatic action of organic preparations and, similarly, of the benefits from transfusion of blood.

Whilst hitherto the application of these principles has been largely empiric, recent advances in our knowledge of organotherapy enable us to command "a substituting hormone therapy, as in thyroid treatment of myxedema; a symptomatic hormone therapy, as in thyroid treatment of obesity; a ferment therapy, as in supplying the finished pepsin or a hormone which stimulates some special secretion, a hormone therapy seeking to utilize the reciprocal and antagonistic action of the endocrine glands, and finally, we have the protoplasma activation therapy as in parenteral protein therapy." (Borchardt.[5])

## Treatment of Individual Syndromes

*Acromegaly.*—Opinions differ widely as to the effects of pituitary extracts in acromegaly, which is due to overactivity of the anterior lobe of the hypophysis. Kuh and Favorsky[6] have noted distinct improvement in the subjective and even the objective symptoms, while Landois and Cesbron[7] used various preparations and for extended periods, and were led to the conclusion that they are entirely ineffective. My own personal experience of the use of pituitary extracts in this disease has not been encouraging. Without doubt, a recognition of the early symptoms of pituitary dysfunction, including commencing skeletal overgrowth, offers opportunity for achieveing the best results obtainable from the use of the desiccated gland. Among these are undue somnolence, aversion to muscular effort, and altered carbohydrate metabolism, as shown at times by anaphylaxis or slight glycosuria ar both.

The synergistic functional relationship existing between the ductless glands is nowhere better shown than in acromegaly. For example, both myxedema and Basedow's disease may form part of the hypophyseal syndrome, as indicated above, the former during the more advanced stages of disease of the pars anterior, as a rule. In cases of acromegaly in which symptoms of myxedema are associated—an expression of functional insufficiency of the pars posterior—the utilization of thyroxin in the treatment in small daily doses, is attended with strikingly favorable results. In two cases of this combination occurring under personal observation, distinctly curative effects were observed from the use af this agent. Not only were

the more characteristic myxedematous deposits removed, but also other distressing manifestations, were in great part relieved, such as the headache, irritability of temper, and insomnia. In the treatment of these two cases, the thyroid preparation was used alone, commencing with small doses which were slowly and gradually increased as the efficiency of the remedy became demonstrated by the results.

In this connection the fact is to be stressed that the use of ready-made combinations before two or more single products have been tried is illogical and tends to hinder rather than to promote progress in organotherapy. In diabetes insipidus, the administration of pituitrin (1 c.c. night and morning) is usually followed by a urine which is normal as to amount and concentration. Per contra, high blood pressure presents a contraindication to the use of extracts of this lobe.

*Myxedema.*—For cases of hypothyroidism there is, as is well known, a sovereign remedy. The necessity for employing thyroxin, in small dosage (gr. 1/80) so as to avoid toxic effects needs to be constantly impressed upon the mind of the medical profession. Suitable measures must also be directed to the relief of any complications and near and remote etiological influences in the individual case. There is a group of cases in which the symptoms entering into the syndrome are less obvious than in typical cases of myxedema. It is sometimes with difficulty that the significant features can be culled from the mass of data at hand, but so-called myxedema fruste presents several at least of the following features: "Irritability of temper, malar flush, apathy, neuralgia, headache, impairment of memory, tinnitus, especially on lying down, slight deafness, slowness of the mental processes, undue susceptibility to cold, weak digestion, constipation, swelling of nasal mucosa, yellowness and slight thickening of the skin and subcutaneous tissues, often confined to certain regions of the body (lower eyelid), early fatigue on exertion and a moderate degree of anemia. The thyroid is usually smaller than the normal. It is to be recollected that in this variety cutaneous eruptions, such as eczema, psoriasis, and urticaria may be present.[8]"

In these mild and earlier stages of thyroid insufficiency, it is not only possible to effect a symptomatic cure, but also to bring about by enjoining absolute rest, a generous diet and the judicious use of thyroxin, a restoration to normal function of the endocrine gland at fault, in some cases at least. Such cases often follow infections or prolonged overstrain and the like.

*Exophthalmic Goiter.*—There is no glandular extract that has a well established reputation in the treatment of chronic hyperthyroidism. Hoppe,[9] however, has shown to his own satisfaction that corpus luteum is highly serviceable and that the patients can thus be kept in a comfortable condition. Careful dietetic, hygienic, and symptomatic treatment should be carried out while this agent is being exhibited. This method of treatment is based on

the assumption of the interrelation between the thyroid and the ovaries in the female and the interstitial glands of the testicle in the male.

In my view a trial should be made of the posterior lobe of the pituitary in selected cases of hyperthyroidism. The thyroid may be observed to diminish in size and the symptoms of the disorder sometimes subside, wholly or in part, as the result of the administration of infundibulin. The effect on the metabolism is noteworthy, slowing the rate, thus favoring the storage of lime salts.

Here it is well to recollect that exophthalmic goiter and myxedema are not, as formerly believed, diametrically opposed to one another in their pathogenesis and symptomatology. Janney and Isaacson[10] have shown that similar metabolic disturbances may be present in both hyperthyroid and hypothyroid states and also that their blood-picture is practically identical. Clinicians should be constantly on the lookout for certain symptoms of myxedema in association with those characteristic of the hyperthyroid syndrome. For example, the presence of some of the features mentioned above may be noted and should lead to the judicious use of a thyroid gland preparation. The effects produced in carefully selected cases are truly remarkable in my experience.

*Hypoadrenia.*—The syndrome associated with both acute and chronic adrenal insufficiency has received much recent attention. The former manifests itself suddenly in diphtheria, typhoid fever, influenza, severe measles, malaria, scarlatina, and other acute infections in "rapid syncopes, with hypothermia and asthenia resembling shock." Maranon[11] has found small suprarenals with little adrenalin and cholesterol at autopsy. In these cases in which collapse is found adrenalin extracts of the whole gland, 3 mg. four times daily, should be administered. In severe types, adrenalin administered hypodermically (dose 0.5 mg. every 2 hrs.) is to be used. In the collapse of an etherized individual or one who has lost blood, larger doses than are usual, 5 to 6 mg. administered subcutaneously, are demanded.

In chronic types of hypoadrenia of suprarenal origin, 5 mg. of adrenin per day is indicated. The drug should always be administered in fractional doses at regular intervals throughout the twenty-four hours. "The injections should never exceed 0.5 mg. at any one point, though as much as 2 mg. can be given at one time." (Sergent). The writer has found the use of the desiccated gland administered *per os* without effect in some cases and in such advises a trial of adrenalin by the subcutaneous route.

In conclusion it is desired to state clearly that there are many uses of the glandular extracts in as many widely different conditions in regard to which our knowledge rests on sure foundations, but these do not fall within the scope of this article. I have considered in detail only certain aspects of substituting hormone therapy and the antagonistic or reciprocal therapeutic application of the glandular extracts. I have also endeavored to suggest

principles, which should govern us in making use of these medicinal agents, rather than a complete discussion of all phases of the subject, which would be impossible within the time limit of this paper.

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## THERAPEUTIC USES OF PITUITARY GLAND SUBSTANCE

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During the last few years the study of the pituitary gland has advanced with extreme rapidity, and, as is usual when this is the case, there has been a great deal of misconception, physiologically and pathologically, regarding the gland, and considerable looseness and inaccuracy in its therapeutic administration.

That the pituitary gland is probably the lead-horse of the endocrine system seems to be indicated by the fact that it is necessary to life, that it is of major importance in the regulation of stature, of adolescent change, of carbohydrate metabolism, and that it is the most protected, in situation, of all the organs in the body.

It is not the purpose of this paper to go into the anatomy and physiology of this gland except to say that when we consider pituitary therapeutics we must bear in mind that the secretion of the anterior lobe has, physiologically, to do with skeletal and genital development, and the posterior lobe, including the infundibulum, with carbohydrate metabolism and unstriped muscle-fiber tonicity. The whole gland combines these functions. There are many other subsidiary functions which may be attributed to one lobe or the other.

When we consider the pituitary secretion we must ascertain whether an

especial lobe, or the whole gland, is oversecreting or undersecreting. We must divide secretory changes of the anterior lobe, which has to do with osseous and genital development, and also of the whole gland, because the anterior lobe is implicated, into preadolescent and postadolescent changes. In considering changes in the posterior lobe secretion this division is not necessary because the posterior lobe, including the infundibulum, does not control the adolescent changes of skeletal and genital growth. We should also try to determine whether any change in secretion is chronic or transitional in character.

Certain tests are useful in the consideration of pituitary cases and we may be aided by a sugar tolerance test and blood sugar estimation. Another test, known as the pituitrin test, is used, but it has not been done over a sufficient period of time to draw definite conclusions.

Radiography of the sella turcica is of very definite importance. In all cases in which the pituitary is radiographed it is well to take both the flat and stereoscopic plates. The changes found vary greatly in the normal cranium but there are certain changes quite indicative. Hypopituitary changes consist of clubbing and enlargement of the posterior clinoids and, at times, they may actually bridge across the sella and meet the anterior clinoids. There may be seen in some cases roughening and filling in of the dorsum sellæ. Thus we have space-restricting encroachment of the sella, limiting, we believe, the secretion of the gland. In the *hyper* cases the sella is enlarged, the floor is smooth, the processes are often spread out, and, not infrequently, the processes are partly absorbed. The sphenoid and frontal sinuses in the hypo cases are usually small and in the hyper cases large. There are also various changes in the hand and other bones which we will not take time to consider.

In the investigation of abnormal pituitary states we should not forget that the gland must not be considered alone, and that the sugar disturbance of pituitary states is related to, and may be confused with, the carbohydrate metabolism of the pancreas. We know that the posterior lobe has to do with blood pressure, but this must also be considered with the state of the suprarenal glands, and the cardiovascular apparatus. Body hair distribution is partly a pituitary function, but the suprarenals and the gonads are also concerned with hair distribution. The pituitary helps to regulate body growth, but so does the pineal gland. We should remember that both pituitary and thyroid states have to do with moist or dry skin, oily or dry hair, loss and gain of weight, and with nervous poise. We must also realize that when the pituitary gland is affected other of the endocrine glands may be disturbed because of its affection, while, on the other hand, some other gland may be affected and alter the pituitary secretion. Hence, any endocrine gland disturbance is, through hormonic action, polyglandular.

Much confusion disappears if we can satisfy ourselves by clinical and radiographic evidence that the pituitary is the gland paramountly affected.

I approach the subject of the details of pituitary therapy with a considerable degree of hesitancy because it is still in the formative stage, but, on the other hand, unless our views and experiences are disseminated they can neither be controverted nor adopted.

The physiological importance, and hence, by inference, the therapeutic potency of pituitary gland substances may be imagined when we consider that a few drops of pituitrin will precipitate the birth of a human being into the world from an inert uterus, while the internal secretion of this gland determines whether the man is to be a dwarf or a giant, changes him from a youth into an adult and may make an individual an effeminate man or a masculine woman. It may deform our features, alter our personality, upset our emotions, blight our mentality, throw us into convulsive seizures, or destine us to be a corpulent and jovial Falstaff or a hairy, aggressive Esau.

In conditions of *over*secretion our therapy is blocked, unless there proves to be some value in treatment by x-ray flashes which is being tried out, save by surgery or the administration of other ductless gland substance which would tend to maintain an hormonic balance. In the case of surgery sella decompression has been practised, but its indication is not definitely determined. It is true, of course, that Cushing, and others who have followed him, have made the removal of pituitary tumors a comparatively safe brain operation, but this paper is concerned only with the medical aspect of the subject. In the case of the antagonistic action of other gland substances, we have not advanced, as yet, far enough in our understanding of endocrine hormones to lay down definite rules of therapy.

It is in the study of states of *undersecretion* of the gland that we may speak with more positiveness, and, in certain instances confidently predict our results. Among the less frank hypopituitary states may be placed acromegaly and the pituitary adolescent psychoses.

*Acromegaly*, as we know, is accompanied by hyperplasia of the bony parts, especially the zygoma, superciliary ridge, hands, and feet. The soft tissue, in certain places, is enlarged, the hair is coarse and dry, the complexion is sallow, the hands are spade-like in shape, and polyuria, polydipsia, glycosuria and various subjective sensations are frequently present. Acromegaly is sometimes a symptom of pituitary tumor, at other times there is a hyperplastic condition of the gland itself. Acromegaly is usually seen in the adult, and the writer feels that there may be present an over-activity of the anterior lobe and normality or under-activity of the posterior lobe. Pituitary therapy in these cases is chiefly symptomatic and confined to the administration of the posterior lobe extract.

*The psychoses of hypopituitarism* usually occur during adolescence and may be preceded by a preadolescent hyper-, normal or hypo-pituitary state.

During adolescence, frequently due to illness or injury, a marked diminution of pituitary secretion takes place and the patient has so much psycho motor retardation that the condition resembles dementia præcox. Repetition of movement is common, as are drowsiness, slovenliness, and inability to concentrate attention. Some patients show truancy, wanderlust, bizarre behavior, and at times hallucinations.[1] Whole gland pituitary extract has cleared up some of these cases.

*The frankly hypopituitary states* should be divided into two classes, the chronic or static, and the transitional. In the static cases there has been evidence of undersecretion of one or the other of the lobes, or the whole gland, since early childhood, and in the transitional cases, usually following illness or injury, there is a more or less sudden let down in the pituitary secretion.

*Pituitary Epileptic States.*—In 1914,[2] 1916,[3] and 1919,[4] I published papers on pituitary epilepsy. In these studies it was found that convulsions, in no way distinguishable from those of so-called idiopathic epilepsy, occur from undersecretion of the pituitary gland. To make the diagnosis of pituitary epilepsy three essentials must be borne in mind: (1) The convulsions must make their appearance during the period of adolescence. (2) The case must present clinical evidence of hypopituitarism. (3) Radiographic evidence of pituitary undersecretion must be present. Of seventeen static cases of this character which have been studied over a period of years we find that in nine of them no attacks have occurred for over three years. Four cases have been taken off of all medication for several years and the attacks have not returned. Two of the remaining cases seem definitely controlled by pituitary feeding, four were improved to some extent, one was not improved but had a bad family history, and one was lost track of. Of the eleven transitional cases reported in 1919 the results were not nearly so striking and it was found that they did not take the medicine as regularly. However, definite improvement occurred in eight of the cases. As a rule the whole gland extract was given in doses of from six to twelve grains daily. In certain cases of genital and skeletal developmental delay the anterior lobe is more effective. At times oral feeding is reinforced by hypodermic administration.

*Obesity.*—Obesity should be treated, after a pituitary diagnosis is established, by careful pituitary feeding of the posterior lobe, or at times of whole gland in those cases which have also skeletal and genital underdevelopment. In these cases it is often necessary to combine either thyroid or ovarian extract with the pituitary. Pure pituitary obesity gives breast-girdle and flank fat and a rounded contour over the pelvic girdle, while ovarian obesity is marked by excessive trochanter fat. Under the heading of pituitary obesity may be placed the condition known as adiposis dolorosa which occurs during postadolescence and is characterized by rolls or cakes

of fat that are painful upon pressure. These cases do not respond so well to endocrine therapy as those of simple obesity.

*Pituitary Headaches.*—These are deep seated, bitemporal headaches, the location of which is frequently described by the patient with the gesture of putting the forefingers to the temples and pointing them toward each other. These headaches may be transient or continuous. The patient may feel as if a marble or some other object is moving about at the base of his cranium. Pardee described these headaches in 1919.[5] At times the sella turcica is constricted, or the gland may swell and stretch the capsule, and pressure may even be exerted upon the cavernous sinus. An upper temporal quadrant restriction of the visual fields may be found. The headache usually ceases upon feeding whole gland pituitary extract. These headaches not infrequently follow some infectious disease and may be due to a toxic condition or inflammatory congestion of the gland.

*Diabetes Insipidus.*—Barker and others have called attention to the relation of the syndrome of polydipsia and polyuria to undersecretion of the pituitary gland. These symptoms are usually promptly relieved by daily hypodermics of posterior lobe liquid. Pituitary whole gland extract by mouth has been used, but is not generally considered satisfactory.

*Dysmenorrhea, scanty menstruation, amenorrhea,* and *menorrhagia* are frequently relieved by the administration of whole gland pituitary extract; or at times a liquid preparation of the anterior lobe is more effective, especially in early adolescent cases. This therapy is often rendered more efficacious when conjoined with the administration of ovarian extract.

*Constipation* due to loss of bowel-wall tonicity is helped by the administration of a posterior lobe preparation. The same is true of inertia of the bladder.

*Enuresis,* due to weak bladder walls, is often of pituitary origin and may be controlled by whole gland feeding or the administration of posterior lobe liquid.

*Backward genital and skeletal development* may be helped by the administration of anterior lobe extract or liquid. If the case has obesity in addition it is best to give the whole gland.

*Reversion of sex characteristics* is usually a combination of pituitary and gonad difficulties and has to be treated according to the physical and metabolic characteristics of the individual case.

Cases of true *dwarfism* and *gigantism* are not usually influenced by pituitary therapy.

*Arterial Hypertension.*—Englebach of St. Louis[6] suggests the use of posterior lobe pituitary extract, in combination with other ductless gland therapy as indicated, to reduce the blood pressure in cases of vascular hypertension not due to cardio-vascularrenal conditions, acute infections, etc.

In conclusion, we may feel that while much pituitary therapy is un-

determined, there are many definite conditions known, in which, when clinical, radiographic, and laboratory evidence is present, pituitary administration accomplishes what nothing else will. On the other hand, the habit of giving pituitary and other ductless gland substances carelessly or empirically should be vehemently interdicted.

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## DISCUSSION

Dr. Oliver T. Osborne of New Haven said the subject of the physiology of the endocrine glands and of the symptoms of their pathology, and the therapeutic value of their extracts was of so much importance and created so much interest, that very much had been written and said with too much enthusiasm and without scientific proof. There was no question that the child, man, or woman was physically and mentally what the secretions of his or her endocrine glands determined. It had been clinically and experimentally demonstrated that the secretions of some, at least, of the endocrine glands were essential for the human being to be normal. However, physicans and even the laity were unfortunately becoming over-enthusiastic in the use of glandular extracts and of glandular mixtures, concerning the activities of which they knew but little, and even patent medicine advertisements were now lauding the use of monkey or other gland materials. Before deciding that a glandular extract was indicated, one must investigate the whole life history of the individual, noting development in all its details from babyhood, though childhood, puberty, and adult life, to the changes from forty-five to fifty, and to senility. The hair, the teeth, the nails, the skin pigmentations, mental activity, the digestion, the blood-pressure, and the character of the circulation all would give indication of the sufficiency or insufficiency of one or more glands. It should also be recognized that the glandular functions were interlocking, and deficiency of one gland might cause deficiencies or hypersecretions of other glands, and the symptoms or conditions present were the outcome of these several disturbed functions. Therefore, to administer empirically a single, or several glandular extracts to a patient, without the most careful supervision or without the understanding that undesired activities might be developed, was

inexcusable. On the other hand, from the very nature of these glandular tissues and the fact that the laboratory, even by extirpation, could not always develop positive chemical or hormone values of the glands, necessitated well directed clinical studies. In other words, many of the valued uses of these extracts had been discovered by clinical trials. The endocrine glands that had been proved to have positive therapeutic value were the thyroid, parathyroid, pituitary, suprarenal, and corpus luteum. Other glands that had therapeutic values, which, however, were not so generally recognized or accepted, were the ovaries, testicles, and mammary. All of the other several docrine gland and organ extracts were as yet subject to a longer clinical proof before they could be accepted as meeting definite indications in the treatment of diseased or disturbed conditions. The pituitary gland was primarily of more importance to the female than to the male, while the suprarenal glands were primarily of more importance to the male than to the female. The pituitary, in conjunction with the thyroid, increased in size and hypersecreted just before, or during the first part of menstruation, and some of the headache of women at these times was due to the congestion of the pituitary gland. As the speaker had pointed out very many years ago, the first, so far as he was acquainted with the early literature, mammary gland extracts when fed to young girls who flooded at their menstrual periods or who menstruated too frequently would inhibit this condition. He also pointed out many years ago that the disturbances of the menopause were largely due to disturbances of the glandular secretions, and that if the thyroid ceased its periodic increased activity at the time the ovarian glands diminished their activity, the hot flashes, nervous disturbances, palpitations, etc., would not occur. On the other hand, if the thyroid diminished its activity too rapidly or too completely, the woman rapidly added weight and showed other signs of hypothyroidism. Thyroid treatment was needed when these latter symptoms were present. Sometimes there was a decided loss of tone in women at this period in which ovarian substance frequently acted as a stimulant and was beneficial. Also ovarian extracts were of value at any period when menstruation was scanty or occurred only at long intervals. The corpus luteum was certainly a distinct gland although it was located in the ovary. It was a stimulant to the uterus and caused its mucous membrane to become ready for pregnancy, or if conception did not occur, allowed the usual uterine flow. Although this gland was frequently administered with success in amenorrhea, he did not believe that it caused ovulation and consequent menstruation, but it did cause the uterus to be ready to bleed. This gland was enlarged and theoretically should be doing more physiological work during the first three months of pregnancy, although the woman normally did not menstruate. Its secretion might be the stimulant that caused the placenta to grow properly. Corpus luteum had been frequently administered for the high blood-pressure that occurred in women at the time of the menopause, and with some success; but it was a potent glandular substance, and might lower the blood-pressure more than was desired. In other words, one must watch the results with corpus luteum administration as carefully as with thyroid. During periods of amenorrhea, or at the time of the menopause, or perhaps some time later, pigmentations were likely to occur, forgotten freckles became prominent, and moles developd. These seemed to evidence a disturbed adrenal secretion, probably of the medullary portion of the adrenals. At present the speaker was studying clinically the activity of extracts from the cortical portion and extracts from the medullary portion of the adrenal glands. But administering

the substance as a whole would not only many times stop this tendency to pigmentation and clear up brown spots, but would also cause improvement in the circulation, when there was low blood-pressure. Finally, he would be very careful in polyglandular therapy, much as we should be careful in advising or using polyvaccines.

Dr. Charles E. de M. Sajous of Philadelphia said that he could emphatically subscribe to what had been said about the empirical use of organic products. Only recently he had seen a New York lady, whom he referred to Dr. Satterthwaite. Although a very bad case of mitral disorder, she had been given thyroid by a physician previously seen. If persisted in, death would probably have ensued. As consultant of the Bell Telephone Company the speaker had had occasion to see many cases of exophthalmic goiter and hyperthyroidism. In one case with bulging eyes and prominent thyroid, the patient had been seen by fifteen doctors in succession and had been treated for cardiac trouble owing to the arrhythmia; not one had recognized the true condition. Between the promiscuous use of organic products on the one side and the non-recognition of endocrine disorders on the other, much poor work was being done. In respect to pluriglandular therapy, a word of caution was offered in view of the gunshot prescriptions that were being given for various conditions—a renewal, in a measure, of the old polypharmacy methods. The speaker urged that no glandular product should be administered without taking into account what glandular stigmata each case presented. There was no doubt that today the profession possessed a very distinct therapy for all endocrinopathies and the general diseases they complicated; but the syndrome could be detected in each case and there was no reason why pluriglandular treatment should be used unless it was indicated by a pluriglandular syndrome. A feature that had not been referred to was the combination of some gland treatment with the usual remedies, strychnine, digitalis, etc. In cases of secondary anemia, for instance, after finding out the cause and eliminating it, one would obtain better and prompter results by adding a small dose of adrenal gland or posterior pituitary and strychnine to the iron, the constituents of the hemoglobin molecule being thus supplied. Concerning immunology, Dr. Sajous felt that many cases were being sacrificed today because the relationship between the thyroid and the immune chemistry of the body, now fully recognized on the continent of Europe, was neglected. He was confident that if surgeons realized more what the thyroid meant they would not remove thyroids as freely as they did. Medical treatment was slower, but it preserved a defensive organ. Although he treated many such cases he had never had to send one to a surgeon, and had had no deaths so far. Others had obtained similar results. Some of his cured cases had been sorely tried during the war and stood the test without recurrence. One of these patients, a Canadian lady, who had suffered from one of the worst cases of exophthalmic goiter he had ever seen, had had four sons at the front during the entire war and had gone through great anxiety and distress, and yet had remained perfectly well. His treatment, published in the Medical Record of September 27, 1919, was based on the recognition of the importance of the relation of the thyroid gland to the immune chemistry of the body. The essential point was to find out what the thyroid gland was fighting and to eliminate it, and to avoid what, to him, was virtually a criminal method, the "symptomatic treatment" carelessly recommended by many authors. As for acromegaly, Dr. Sajous was always ready to yield to *bona fide* evidence, but he had not changed his mind to the effect that the pituitary gland was not a secreting organ, and before

very long he would adduce ample evidence to that effect. He had patiently awaited the believers in the secretory theory to prove the existence of a secretion, but it was increasingly becoming evident that the so-called secretion was a myth, as the speaker had long urged. Taking, for instance, the supposed relationship between the anterior pituitary body and growth based upon the prevailing conception of acromegaly: Had any one present ever caused a dwarf to grow by giving him anterior pituitary? Even tethelin had completely failed in this respect. And yet other glandular products had sometimes been found very efficient in this respect when the cause of the arrest of growth could be determined. All were familiar with the connection between pituitary disorders and polyuria, but did they realize that this condition could also be caused by passing a needle into the basal tissues behind the pituitary, cutting off the splanchnic, i. e. along the pituitoneural path Dr. Sajous had long ago described? Every one had been dazzled by Cushing's beautiful book, but this brilliant surgeon had not studied phylogeny far back enough or he would have found a close relationship between the sympathetic and the posterior lobe of the pituitary body, which, through the pituitary neural path, influenced the adrenals and other endocrines. The secretory theory had started as a mere assumption and was dying fast—a good riddance which had been misleading able workers for several decades. Dr. Sajous said that if any one had seen his cases of acromegaly when they first came under treatment based upon his conception and two months afterward, they would have been astonished by the change. The faces gradually flattened down as far as the bones would permit. Was it through glandular therapy? No; through vasocontraction. He considered acromegaly as a vasoneurosis due to a lesion of the anterior pituitary capable of inhibiting more or less the coordinating functions of the neural or posterior lobe.

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## MORBIDITY AFTER OPERATIVE TREATMENT IN ABDOMINAL SURGERY

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Those who take the trouble to reexamine patients from time to time after abdominal operations must be impressed by the rather large percentage in which there is no relief from the symptoms. After operations upon the stomach, duodenum, and biliary system persistent symptoms are distressingly frequent. After operations for chronic appendicitis pain and tenderness in the right lower quadrant are not unusual, and operations for displacements of the kidneys and uterus not infrequently fail to relieve the backache and supposed reflex symptoms for which they were performed.

Three facts stand out as one contemplates these failures of operative treatment: (1) The cause of the original symptoms was extraabdominal and operative treatment was a therapeutic mistake. (2) An intraab-

dominal lesion giving symptoms was present, but was not recognized by the operator and the wrong operation was performed. (3) The operation was a technical failure, because it either failed to do what was intended, or added new pathological conditions that caused a continuation of the old or implanted new symptoms.

Especially important are the cases falling in the first group in which abdominal symptoms leading to operation originate without the peritoneal cavity. Much has been written about the acute peritoneal symptoms produced reflexly in disease of the thorax. An acute right lobar pneumonia with pleuritic extension causing a reflex spasm of the muscles of the right abdominal wall with pain referred to the abdomen is a not uncommon picture. In a central pneumonia with extension to the diaphragmatic pleura, the physical signs of the pulmonary disease may be difficult to elicit; but if we recall that appendicitis begins with diffuse abdominal colic, followed by nausea and later by localization of pain, with tenderness, and elevated temperature appearing as the last symptom, while chill, increase of temperature, and pain are initial symptoms in pneumonia, we will often avoid error; while the disproportionately rapid breathing, the expiratory grunt, and the early thoracic signs should immediately counteract the impression produced by the associated rigid abdominal walls and possible vomiting. Unfortunately, the nerve reflexes in the abdomen have been unduly emphasized. We must remember that pneumococcic or streptococcic peritonitis is a not infrequent accompaniment of pneumonia or pleurisy. The primary rigidity of the abdomal wall disappears to be soon followed by recurrent vomiting, tympany, intestinal obstruction, evidence of free fluid, perhaps without muscular spasm. Operation or autopsy shows an often unsuspected diffuse purulent peritonitis in these cases. In chronic irritation of the pleura, and in non-inflammatory transudations in the pleural cavity, the chief pain may be referred to the upper abdomen on the affected side. Without an examination of the chest the consultant may be led to consider biliary, gastric, or some other form of upper abdominal disease as the cause of the symptoms.

Of the more chronic affections, the gastric symptoms of pulmonary tuberculosis have led to many useless operations, especially for gastric ulcer. Frequently the chief complaint of the patient is gastric distress, often apparently increased by taking food and associated with vomiting. Not infrequently the patient says he has vomited quantities of blood, and the cough and other respiratory symptoms are so slight as not to attract the attention of either the patient or consultant. In young women especially and also in young men who give symptoms of a chronic or subacute gastric ulcer, the thorough study of the chest is much more

important than a fractional meal, and well made radiograms of the chest are often more illuminating and less subject to error than the roentgenological study of the stomach. Someone has said that we may depend upon the *x*-ray evidence as to ulcer of the stomach in 10 per cent. of the cases. Personally, I have found that ulcers apparently shown by the *x*-ray plate or fluoroscope, but not clearly confirmed by the associated clinical symptoms, can rarely be demonstrated by operation. Unless the roentgenologist has unusual skill, is a good clinician, or is a lucky guesser, you will often find that hearing and not seeing is believing, that the history tells more than the fluoroscope. If you ignore the chest and depend on the average roentgenologist for your diagnosis, you may operate in many cases for gastric ulcer when the lesion is pulmonary tuberculosis.

Besides the evidence from the thoracic examination, the patient with pulmonary tuberculosis usually has a true anorexia, an aversion for food, while the patient with ulcer has hunger and eats to obtain relief or to satisfy his appetite, or refrains from eating because of symptoms, such as pain or vomiting that he knows will follow. Mayo Robson estimated that 20 per cent. of patients with gastric ulcer develop tuberculosis. Probably it is more correct to say that in over 20 per cent. of the cases the gastric symptoms indicate pulmonary tuberculosis.

I find I have been prone to forget that attacks of severe epigastric distress occuring often at night with nausea and at times vomiting may indicate a serious myocardial lesion, an aortitis, or disease of the coronary vessels, rather than gallstones or cholecystitis. As a rule, the patient is of middle or rather advanced age, usually obese, and on casual examination the heart sounds heard indistinctly through the thick walled chest may be considered normal or nearly normal. Often the patient is referred to the surgeon with the history of having been treated for months or years for a chronic digestive disturbance, often the internist recognizes the existence of cardiovascular trouble, but insists that operative relief for the very evident and distressing gastric symptoms be given. Possibly there is history of a previous operation. And with or without operation the patient's sudden death may occur in a nocturnal attack or the patient may instantly die under sexual or other excitement. When the usual symptoms of angina are present, the diagnosis is more obvious. If an operation, such as a cholecystostomy or cholecystectomy is done, the patient may greatly improve, due to the rest in bed and perhaps also the other restrictions that follow a serious abdominal operation. Unfortunately, with the resumption of the usual mode of life, the old symptoms recur and an excuse is sought—"Adhesions, too short a period of drainage, failure to remove the gall-

bladder"—for the poor surgical result. Robert H. Babcock has pointed out how the myocardium may suffer from a septic focus in the gall-bladder or appendix. The converse is perhaps more frequently true—that with a passive congestion of the liver and stomach from a failing myocardium changes with at times associated infection involving the bile and gall-bladder are not uncommon. We believe that myocardial disease advanced enough to give marked upper abdominal symptoms will rarely be permanently relieved by operation on the gall-bladder or appendix. This is not asserting, however, that a cholecystectomy or appendectomy fifteen years before might not have eradicated a septic focus and might not then have prevented or relieved the myocardial disease.

Gastric attacks due to endocrine dyscrasia or general metabolic disturbances, such as that commonly described as "bilious sick headaches," or as acute bilious attacks, are not amenable to the usual abdominal operations. Likewise, backaches due to toxemia, faulty static conditions, spinal disease, sacroiliac relaxation, will not be relieved because a retroverted, or fibroid uterus is corrected, or because ptosed kidneys are decapsulated and sutured. Neurotic patients, many of whom have merely the toxemias of an unrecognized pulmonary tuberculous, or other infection, of course will not be benefitted by an abdominal operation, when the causal element lies without the abdomen. While we are more careful to avoid operations on the stomach for symptoms produced by lead colic Pott's Disease and tabes, it is not generally known that the early root pains in encephalitis lethargica may result in the admission of patients to surgical wards for acute appendicitis or cholecystitis.

In the second class of patients, where the predominant abdominal leesion is not recognized, or treated at operation, we find a sufficient number of patients to emphasize the importance, when operating, of examining and recording the condition of each organ in the abdomen as often as the exigencies of the case will permit. Too often reoperation is rendered necessary by the carelessness or error of the first operator. Gastric symptoms, reflex from an encapsulated pelvic abscess or old ectopic pregnancy, will not be relieved by a gastroenterostomy. An appendectomy will not help ureteral colic, nor will the removal of small uterine fibroids cure an annular carcinoma of the splenic flexure. A careful intraabdominal exploration with the gloved hand may save the patient from being sutured after the removal of an innocent appendix, when gallstones or gastric ulcer are present. It is to be recalled that a slight evening elevation of temperature and progressive loss of weight and strength may be the only symptoms elicited from a hypernephroma

of the kidney. A mobile cecum and ascending colon are frequently overlooked and may cause persistent distress after an appendectomy or other abdominal operation.

The ascending colon should be a fairly fixed standpipe, for here 80 per cent. of the water of the food is absorbed. If it develops a mesentery and slumps down, its capacity is reduced and its attachments are such that it tends to drag down the right kidney, the gall-bladder, and the duodenum. Thus, as has been emphasized by Waugh, appendiceal, renal, biliary, and gastric symptoms may follow. We are inclined to think that neglect of this portion of the bowel has given us a considerable postoperative morbidity. It is not difficult to restore the fixity of this portion of the colon, or by plication to shorten and decrease in size redundant portions of the bowel.

In the third class, among the operations that fail to do what was intended, we would mention the removal of epiploic appendices in mistake for the vermiform appendix; the partial removal of the appendix with retention of an infected stump or of overlooked fecal concretions that have escaped from the appendix; operations for visceroptosis that fail to hold or give symptom producing adhesions; incomplete removal of sources of infection, as a simple amputation of the Fallopian tubes when there is chronic gonococcic infection of the endometrium. The drainage of a diseased gall-bladder is often followed by symptoms, as is a cholecystectomy, with obstruction of the common bile duct, or a choledochotomy with retention of a stone in the ampulla of Vater.

Too often we fail to individualize in our operative treatment and instead of doing the logical thing for the particular case blindly follow our own method or that of some brilliant teacher. How many of us take into account when we attempt a gastroenterostomy that the operation tends to lower acidity, motility, and the emptying of the stomach, and to increase greatly the irritation of the jejunum and the likelihood of jejunal ulcer, and that with an open pylorus, it is to a very limited degree a drainage operation. It is true that there are exceptions like the "dumping stomach" from gastroenterostomy described by Andrews, but such exceptions also produce troublesome pathological changes. Surely a chronic ulcer with wasting of the peptic glands, low acidity, and low motility is not to be treated like an acute ulcer with high acid values and marked motility; yet do we discriminate as we operate?

We are now constantly trying to eliminate the pathological results of such makeshift abdominal operations as gastroenterostomy. We must turn from pathology-producing operations to a more earnest attempt to restore physiologic function in our surgical treatment.

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## DISCUSSION

Dr. F. M. Pottenger of Monrovia, Calif., directed attention to one point in regard to pain after diseased conditions had been cleared up, which had not been sufficiently appreciated because our conceptions were anatomical instead of physiological. When an organic lesion was removed, the nerves were not restored to their former power of resisting impulses. Women with uterine troubles, patients with tuberculosis, pleurisy, or chronic appendicitis might be relieved of all these troubles, yet if they should be worried or tired out they would still often have their pains because the threshold of response in the neurons was lowered so that the impulse passed more easily than normal. One might remove the organ or the disease, but the patient's nerves were still not restored to normal.

Dr. Hyman I. Goldstein of Camden, N. J., said that in this connection it should be remembered that some very good surgeons were too apt to accept the diagonsis made by referring physicians. In some of these cases, were the surgeon and staff to reexamine the patients more thoroughly, some of these operative failures might be avoided. He then cited a case with attacks similar to those mentioned by Dr. Babcock, with acute indications and symptoms such as vomiting, epigastric pain, etc. After thorough Roentgenographic study the patient was operated upon under the suspicion of possible ulcer, but no ulcer was found, nor anything abnormal; the usual procedure of appendectomy was followed, and the patient felt a little better for a time. Four to six weeks later he again had severe vomiting and epigastric pain. The blood Wassermann was negative and there was no history of any initial lesion. Later the pains became worse, and it was decided that possibly he had adhesions following the first operation. He was again subjected to operation and nothing seriously abnormal was found. Subsequently the spinal fluid and blood Wassermann was found to be strongly positive. In the meantime the patient had had several of these seizures. After the second injection of neoarsphenamine the man, for the first time in eight years, had no seizures, and further treatment practically cured him.

Dr. Fussell of Philadelphia reported two cases of acute pericarditis which simulated acute appendicitis, at a recent (May 30, 1921) meeting of the College of Physicians of Philadelphia, section on General Medicine. Some years ago Dr. Libman of New York City reported cases of primary sarcoma of the intestines, simulating appendicitis, while last year the speaker reported a case of primary sarcoma of the appendix with intestinal obstruction by a band that simulated acute appendicitis.

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# THE TREATMENT OF EPILEPTIC MANIFESTATIONS IN CHILDREN FROM THE STANDPOINT OF THE CONSTITUTIONAL BASIS.

By E. BOSWORTH McCREADY, M.D., F. A. C. P.
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For centuries the pathogenesis of idiopathic epilepsy has been one of the baffling problems of the medical profession, consequently therapy has been principally directed toward the suppression or mitigation of the

convulsive crises, consisting for the most part in saturation with depressant drugs, which, "while reducing the number of seizures, simultaneously aggravate the morbid process."

Adequate proof of the exact nature and cause of this frequent and fearsome disease is still lacking. While in many epileptics coming to autopsy definite pathological brain tissue conditions can be demonstrated microscopically, the character of the changes differs widely as observed by different investigators, some describing a generalized gliosis, others, areas of sclerosis in different parts of the cortex, while still others have observed degenerative changes in the ganglion cells. The existence of these lesions does not prove, however, whether they are the essential cause of the epilepsy, whether they are developmental (hypoplastic) in origin, acquired, or are the result of the epilepsy. The theories of Clark as to the psychogenetic element in the convulsions are applicable to a small percentage of epileptics and of significance in the inauguration of occasional attacks in others. It is thought by many observers that the epileptic attacks are due to the accumulation of toxic wastes in the blood. Sajous strongly supports this view and contends that such accumulation is due to inherited or acquired hypoactivity of the adrenal system, particularly the anterior pituitary as test-organ. The investigations of Johnston, McKennan, Tucker, and Munson upon the sella turcica and the pituitary would seem to lend strong support to the theory which assigns to the pituitary body an important place in the etiology.

The epileptic is usually the product either of a "bad heredity" or of unfavorable gestational and environmental influences or of a combination of both. The same influences that operate in the production of constitutional inferiority (degeneracy or hypoplasia) in general are responsible for the epileptic constitution. These may be briefly summarized as:

1. Hereditary: Due to defects in the chromosomes of the germ cells of parents.

2. Environmental: Due to toxemia from various causes in parent or parents affecting the germ cell or cells, resulting in a defective impregnated germ, or to toxemia in the mother or to local disease in the endometrium leading to defective or insufficient nutrition of the fetus or embryo.

3. Both hereditary and environmental forms occurring in the same individual.

Any interference with the natural forces of growth by vitiating influences modifying cell nutrition and development tends to become aggravated through the close interrelation and interdependence of the various systems of body cells, among the most important of which are those initiators and regulators of correlative growth—the ductlessglan-

dular and vegetative-nervous systems, and further disturbnace in growth and development results. The structures which were the last, phylogenetically, to develop and to achieve effective complexity, the endocrine, central nervous, and vegetative nervous systems, are most likely to suffer, even though the rest of the soma escape with little injury.

It is pretty definitely established that the endocrine system controls the metabolic processes and presides over growth and development in infancy and childhood; that upon its integrity depends mental, physical, and reproductive efficiency in adult life, and that it maintains catabolic balance during senescence. Thus it is evident that in evaluating the various factors contributory to the epileptic constitution the endocrine system must be given serious consideration. The writer has failed to find any constant and peculiar endocrine anomaly in epileptic children, nor has he found any essential difference in the endocrine abnormalities of inferior children with epilepsy and those who have never had convulsive attacks, yet varied manifestations of endocrine imbalance are common in these patients and the highly satisfactory results following treatment, in properly selected cases, by organotherapeutic measures, is in his mind significant evidence as to the implication of endocrine system in the etiology.

As the ductless glands are themselves vegetative organs, supplied by vegetative nerves and possessing central projection fields, their functions are, in great measure, regulated by the nervous system, and in turn the excitability of the nervous system (the vegetative, particularly) is influenced by the hormones which the endocrine system gives off to the circulation. Thus we frequently find definite indications of vegetative nervous disequilibrium.

The attempts to establish the gastrointestinal system as the prime offender in epilepsy have failed of success. Most epileptics are constipated and the constipation likely has more or less influence (toxic absorption, reflex irritation, etc.) upon the severity of the disease, but it is probable that gastrointestinal anomalies are little, if any, more frequent than in other organically inferior individuals. When these anomalies do exist, however, their treatment by appropriate measures exerts a favorable influence upon the severity of the disorder.

Anemia is an almost constant manifestation of constitutional inferiority in children, particularly in those with epilepsy. The developmental arrest, whether hereditary or acquired, affects the blood-making organs and as a result there is a hemic dyscrasia, which the writer is in the habit of referring to as "hypoplastic blood," blood which is ontogenetically incomplete, resembling the fetal type. The hemoglobin is

low in percentage and is unevenly distributed, the red cells are decreased in number, are irregular in shape and size, and many are nucleated; Myelocytes may be present and usually there is lymphocytosis and an increase in the eosinophiles.

The epileptic child, like other constitutionally inferior children is apt to present anomalies, as visual defects, enlarged tonsils and adenoids, phimosis, impacted teeth, etc., which serve as reflex sources of irritation aggravating the convulsive tendency, sometimes even to the extent of determining the occurrence or absence of attacks; for the epileptic individual can carry without convulsions a certain load of constitutional and functional anomaly, but when the load becomes too heavy convulsions ensue. The aim of therapeusis is both to lighten the load and to increase the patient's carrying power. The affective peculiarities of the epileptic are often apparent from birth. He frets at slight bodily discomforts, or from the mere tedium of existence, is peevish, easily startled by noises, over-sentitive to impressions of all kinds, is self-willed, with extreme lability of mood. While he usually sits up, crawls, walks, and talks at about the usual time, he fails to develop the ability to perform the finer muscular adjustments, and continues to be clumsy and incoordinate. Usually he is hyperenergized, when hereditary factors predominate in the etiology, or alternately restless and lethargic, when developmental arrest is both hereditary and environmental in origin. While epilepsy is often accompanied by a varying degree of mental enfeeblement it is sometimes difficult to determine how much of this is the result of the developmental arrest and how much is deterioration resulting from the fits. The psychic peculiarities of the epileptic personality correspond closely to the degree of developmental arrest of the nervous system and consist, chiefly, of egocentricity, supersensitiveness, and emotional poverty. It is in accentuation of these traits, and in the absence of a sense of inferiority that the epileptic personality differs from the neurotic. The varied manifestations of the instinctive defects are ably and fully treated by L. Pierce Clark in numerous articles..

The rational treatment of epilepsy consists, not so much in suppressing the convulsive manifestations as in removing and counteracting those factors and influences which are of etiological and contributory significance, and by so doing to modify the individual's constitutional reactions. We have seen that the epileptic has an endocrine system, a nervous system, a metabolic system, and a circulatory system of peculiar stamp, and this individual differs in his susceptibilities and reactions to stimuli, physical, chemical, psychic, and social, from beings of normal

make-up. It is especially important that treatment be instituted in early years when developmental trends may be directed and modified.

Recourse to depressant drugs, as the bromides and luminal, should be made only after every other therapeutic aid and corrective measure has been exhausted, or when, for some good reason, it is advisable to suppress the attacks temporarily until other lines of treatment become effective. All sources of reflex irritation and foci of infection should be removed, and their removal is sometimes sufficient to arrest the convulsive attacks permanently, but usually such procedure is but the preliminary to effective treatment.

It must always be kept in mind that our aim is to effect remote rather than immediate results and that we are attempting so to modify the individual's developmental trends—his cellular and chemical constitution—as to lessen his response to irritative factors which ordinarily inaugurate a convulsive reaction. The syndrome of suboxidation characteristic of the disease furnishes definite therapeutic indications. Thyroid in small doses is useful in selected cases and especially in young subjects. The dose, except when definite hypothyroidism exists, which is not unusual, should be very small and very gradually increased or the condition will be aggravated as a result of excessive metabolism. The use of pituitary substance has met with success in the hands of Tucker, McKennan, and others, and the writer has also seen excellent results follow its use, especially in children of the dystrophia-adiposissexualis type. He believes, however, that the endocrine implication is usually pluriglandular and unless contraindicated, uses thyroid, pituitary, suprarenal, and thymus in combination, finding that by so doing he achieves better results than from giving a single gland substance or extract.

Stimulation of the endocrine system to correlative activity is not the only indication to be met. While the endocrine system influences the vegetative nervous system and is concerned in blood genesis, the action is reciprocal and to influence body chemistry effectively we cannot depend upon endocrine therapy alone. Many epileptics show definite symptoms of vagotonic irritability. In these belladonna or atropine is useful, given in ascending doses until the limit of tolerance is reached. It is of the greatest importance to correct the anemia which is practically always present. Several patients under the writer's observation had convulsions only when the hemoglobin fell below 65 per cent. Iron, in spite of recent investigations which serve to discount its value, is, in the writer's opinion, the remedy of greatest value in anemia. It must be given in large doses over a considerable period. Faulty lime metabolism (calcium deficiency) is a natural accompaniment

and possibly an important contributory etiological factor in epilepsy. For the purpose of supplying lime to the tissues the writer uses calcium chloride, or powdered osyter shell and powdered egg shell (rich in calcium carbonate), the membrane being included in the latter because of the supposed action of the contained keratin upon metabolism and development.

While various dietary restrictions have been enthusiastically advocated the writer believes that the epileptic, like other constitutional inferiors, requires a full and well-balanced diet. The withdrawal of salt in those with chloride retention is of advantage for a time, but if long continued impairs the osmotic properties of the blood and retards metabolism. The proteins are necessary to growth, to cell development in its most inclusive sense, particularly are the animal proteins essential to proper blood genesis. While it is sometimes advisable for a time to restrict the proteins when intestinal putrefaction is a factor, to do so indefinitely produces remote effects which are deleterious to the economy. The excess of potassium salts in an exclusive vegetable diet conduces to nerve irritability. The same result, for a different reason, follows a diet deficient in vitamines.

Lack of time forbids the discussion of the hygienic and educational management of epileptic children. Their hygienic needs differ but little from those of other hypoplastic children, which are taken up at some length in other of the writer's contributions. In meeting their educational requirements the psychic reactions peculiar to the epileptic constitution must be given special consideration. It is desirable, and in some cases necessary, that the child be removed from his previous environment. The psychic element in the fits is often an important factor and can best be controlled away from parents, relatives, and friends.

The alleviation of epilepsy is not a matter of a few days or a few weeks, but requires months and even years of careful intensive treatment—medical, hygienic, and educational, and when properly carried out the results are eminently gratifying to patient, family and physician.

**Conclusions.**—1. The convulsive manifestations of idiopathic epilepsy are the result of a dyscrasia which itself is the result of constitutional defect or inferiority.

2. In this constitutional inferiority, the endocrine system, the nervous system, the metabolic system, and the hematopoietic system are involved.

3. Rational treatment should be directed toward the correction of existing anomalies of function and toward the stimulation of normal correlative development, consisting of intensive medical, hygienic, and educational treatment under favorable conditions of environment

4. The plastic period of early childhood is the best time for the institution of such measures.

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## DISCUSSION

Dr. Beverley R. Tucker of Richmond said that one hated to discuss a paper of this kind in five minutes for it contained so much of thought and suggestion that it was difficult to know where to begin or where to stop. One reason that more advance had not been made in the treatment of epilepsy was the assumption of the attitude that epilepsy was a disease. For some time he had reversed that attitude and had taken the position that convulsions were merely a symptom, just as headache or fever. With the older attitude patients usually got very poor examinations and very poor treatment, but if the state was approached from the view that the recurrent attacks were the sympom of some underlying condition, then one was compelled to make a more complete and thorough examination. Age had a great deal to do with the character of the recurrent attacks. Cases beginning in early life were due either to some constitutional inferiority handed down from ancestors or to obstetrical birth deformity. He had seen cases in which children's heads had been photographed with evidences of intracranial pressure. One child had an accumulation of cerebrospinal fluid between two of the sulci in the frontal lobe. There was no cyst wall, simply the cavity between the pia and arachnoid. The accumulation of fluid amounted to an ounce, which was evacuated and the cyst for a time was relieved; later it returned. The pituitary cases usually appeared during adolescence; in fact, he rather hesitated to make a diagnosis of pituitary epilepsy that had not occurred during adolescence. He rather agreed with Dr. MacCready that it was pluriglandular rather than simply pituitary. In fact, he doubted very much whether there was a true one-gland condition; probably all gland conditions were pluriglandular, with one gland paramountly affected. Later cases were found beginning in middle life; that was usually due to variable vascular tension while the patient was getting used to the blood pressure increase. During this period recurrent convulsions in no way distinguishable from idiopathic epilepsy occurred, and sometimes when the blood pressure became stable the attacks spontaneously ceased. This was a small group of cases. A small growing neoplasm or a small hemorrhage (sometimes a hemorrhagic diathesis) would give convulsions. Then, too, it should be realized that a convulsion was a convulsion whether it was single, occurred in a series, or was recurrent, whether it was irregular, or whether it showed periodicity. Convulsions occurred in meningitis, brain tumor, tetanus, eclampsia, etc. These were just the same as the convulsions that occurred in a case of epilepsy. Dr. Tucker said he felt so strongly on this point that he would like to see the word epilepsy dropped altogether from medical nomenclature, for it undoubtedly stigmatized the patient, even in the toxic and traumatic cases; but if one delivered a patient and gave a cerebrocortical defect to a child, and the child had convulsions, the stigma should belong to the physician rather than to the child. He did not pretend to have solved the problem of epilepsy, but he was convinced that if the subject was approached as a symptom, whether recurrent or single, a better understanding of the subject would be gained than had been reached in the last hundred years or so.

Dr. Charles E. de M. Sajous said that the material contributed by the Thera-

peutic Society was so valuable and helpful in every-day work that he hoped the time would come when it should be possible to see the volume of transactions published promptly. There was one feature of epilepsy which he wished to emphasize, for it had enabled him to help to some recoveries. He had been called one night to see a little girl whose convulsions numbered from 30 to 100 per night. She had now been well for seventeen years, although she had gone through three confinements. Recovery was due to the consideration of the intoxication originating in the intestinal canal. One should bear in mind that focal infection in epilepsy was one of its important pathogenic factors. In the study of every case he investigated every possible source of infection or toxemia, besides, as Dr. MacCready had said, any pressure symptoms or history of traumatism. The essential feature, as emphasized by Dr. Tucker, was that we were dealing with a symptom, the cause of which could sometimes be discerned and eliminated. Barium-meal and fluoroscopic determination of intestinal efficiency should be resorted to in every case. In one instance, x-ray examination of the abdomen revealed several calcified glands in the splanchnic area. As Dr. MacCready has also said, there was often an element of anemia in these cases, but also such usually proved to be due to the hemolysis consequent upon a focal infection. When thyroid gland was administered, one should not lose sight of the fact that it acted as a catabolizer and that large doses favored hemolysis. Small doses should alone be given in these cases.

Dr. Jacob Diner, referring to Dr. Sajous' remarks in regard to the earlier publication of the Transactions, said that the action of the Society in increasing the dues would facilitate that end. At the same time, it should be remembered that the papers and the discussions usually appeared within a few months and were available in the Medical Record. If they did not appear before that time it was because the papers were not in the hands of the editor, and an effort had been made to obviate that. If there were such a thing as adopting a slogan for each meeting on bringing out the literature for the meetings, the last meeting and this one would furnish excellent material. At the last meeting emphasis had been placed on the importance of treating the patient and not the disease; and if he had to choose a slogan for this meeting he would choose: Seek the cause and not the symptom. This point had been ably brought out by Dr. MacCready and by Dr. Tucker in the discussion, whereas it was often lost sight of by the practitioner. Certain diseases had been named instead of naming symptoms; and these symptom-complexes had been applied to the diseases so named, instead of regarding them merely as symptom-complexes possibly present in many pathological conditions. If this meeting would do nothing more—it had done much more—than calling the attention of the physician to the necessity of following the French slogan that underlying all manifestations of trouble they should *chercher la femme*, we should have the slogan: *Cherchez la cause*.

Dr. George H. Hoxie of Kansas City inquired in regard to the prognosis of the epilepsy due to pituitary disturbance. In his own work the treatment by the administration of pituitary extract had been very unsatisfactory and he could not see any permanent benefit from it. He questioned the etiology of the disorder as being anything more than a cortical irritation from causes as varied as the number of the cases.

Dr. MacCready requested that Dr. Tucker answer Dr. Hoxie's question, as he had had more experience in that direction.

DR. TUCKER replied that if pituitary treatment was applied to all cases of epilepsy that occurred during adolescence the results would be discouraging; but if the cases were carefully selected, with clinical and radiographic evidence and treatment applied on the first appearance of convulsions during the period of adolescence, as he had indicated the previous day, good results might be expected. Out of 17 cases reported in 1919, 4 at that time had not had convulsions for over 3 years; he selected these cases, thinking it was fairer than the more recent cases. Now, 9 cases had had no attacks for over 3 years and 4 of these had had no convulsions for from 6 to 9 years; two had had pituitary gland substance irregularly. If they took it regularly they would not have attacks; if they dropped it, the attacks would recur. So far as he could estimate, these 17 cases represented only about 8 per cent. of the cases that came to the office in ordinary private practice. The group was small and depended on the selection of cases. One case had been lost track of; another one had been included in the second group, but the patient was found to have three brothers and sisters in an institution, so it was taken out of the adolescent group. He repeated that if the cases were selected one could expect results.

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## DISEASE AS SEEN THROUGH THERAPEUTICS

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In the classical works issued fifteen or twenty years ago diarrhea was mentioned among the symptoms of the prodromic period of typhoid fever. Now, on the contrary, it is admitted that constipation is more usual at that period. These contradictory opinions are readily explained by the fact that formerly every kind of gastric derangement was created by the use of purgatives, and when the gastric trouble was the first sign of typhoid fever, the diarrhea was naturally due to the purgative and not to the typhoid process. This exemplifies disease as seen through therapeutics!

A certain school has been unanimous in teaching that dilatation of the stomach comes on with typhoid fever and follows it throughout. There was a double reason for such a mistake: the diagnosis rested on a most misleading symptom: the gastric ripple. Moreover, the patients were not to be fed. As a rule, when fed during typhoid, they do not show dilatation, which was deemed formerly almost unavoidable. A. Mathieu and J. Charles Roux have shown the causal rôle of insufficient nutrition in the genesis of gastric dilatation in typhoid fever as well as in other diseases. This affords a second instance of the same disease as seen through therapeutics.

This may be emphasized by the following case: A sixty year old patient, on the twentieth day of a typical typhoid fever, established by a

positive serodiagnosis, had developed coma. After she had refused to take any kind of food for the first twenty days, it was found sufficient to feed her for twelve hours on milk and coffee to make her so much better that she could recognize me (I was a very near relative of hers). I was then able to tell the attending physician that we were watching a case of illness seen through therapeutics. My colleague very frankly acknowledged that he had not sufficiently insisted on the diet question and that the coma demonstrated this fact.

We are taught that icteric patients by retention get thinner; I am experimentally certain[1] that when sufficiently fed they do not get thinner and can even grow fatter, even if the icterus persists several months. The statement that all icterics by retention must grow thinner simply means that the patient has been again looked at through therapeutics; emaciation is an artificially created symptom, in which the practitioner has neglected to consider how far anorexia and insufficient nutrition were responsible for it. This view is pregnant with lessons; for, indeed, if a patient suffering from retentive jaundice grows conspicuously thinner, while sufficiently fed, one is justified in considering the case as one of some lesion leading to cachexia, usually cancer. As it is always somewhat difficult to establish the cause of a retentive jaundice, it is important to possess an easy means of laying down, after fifteen or twenty days at most, an almost positive diagnosis, or better, of setting aside the cancer hypothesis, if the emaciation stops or if the patient grows fatter. Whenever I have used the dietetic method described, it has proved true.

In cases of pregnancy, the so-called incoercible vomiting would often cease if a diet appropriate to the dyspeptic state of pregnant women were ordered. The patient is too often left to her own dietetic whims, and her vomiting seems irrepressible. This is an example of ineffectual therapeutics.

Veronal or any other hypnotic taken after the evening meal or on retiring will often act only the next day, so the patient will feel uncomfortable during the daytime. If it had been taken half an hour before the evening meal[2] it would have brought sleep during the night and been evacuated in the morning; so the day would have run smoothly. This affords another instance of therapeutic symptomatology.

How many misdeeds has anaphylaxis been charged with in "accidents which have been ascribed to it without their having anything—or hardly anything—left of the conditions described by Richet" as Marcel Labbé[3] so excellently says; these misdeeds can be safely explained if observation is cleared of misleading agents. The following example about egg-anaphylaxis is, I think, conclusive. Some persons, called "egg-anaphylactics," can digest an egg easily if they use the small

salt-cellar spoon to eat it with. Why this different tolerance? An underboiled egg when too quickly swallowed, curdles in big bits which cannot pass easily through the pylorus and determine indigestion; by using the small spoon, the person must swallow very small quantities of albumen, which break up into tiny curdles on which the gastric juice works better, enabling them to cross more comfortably the pyloric strait. Here again are symptoms seen through an alimentary mistake.

I do not, in any way, deny the existence of anaphylaxis; I only believe and have long believed—as my lectures have shown[4]—that its province has been unduly extended—an opinion which Marcel Labbé[3] equally maintains.

Let us now turn from the clinical department and enter that of experimental physiology.

When I studied, first experimentally,[5] and then radioscopically with G. Barret[6], the passing of water through the stomach, my conclusions differed from those of experimentalists of the first rank (Gley and Rondeau, von Mering and Moritz, Laborde, A. Mathieu, Hirsch) whose unquestionable statements all differed one from another.

An explanation of these divergences is easily afforded. Each experimentalist had been using different technique; the distance of the intestinal fistula to the pylorus was not the same in all these experiments; and that was the only reason why the results differed. Each physiologist's observations were correct, excepting in one feature which I tried to avoid by using another method, namely, avoiding all operation upon the animal and studying the passage of liquids with the aid of the screen.

I only mention these results because they afford an instance of physiology seen through experimentation, and because it might prove useful to compare it with a case of disease seen through therapeutics.

We find in medicine as well as in physiology and therapeutics differences of opinion which are puzzling and discouraging for the physician, and which little by little bring him to believe in nothing. When he begins studying he is taught certain things; later he is told that what was true twenty years ago is no longer true to-day. It is probable that medical opinions would not change so frequently if clinical experimentalists were more accurate in ascertaining the actual circumstances of their experiments. One must acknowledge that this is a more difficult task for a physician than for a physicist or chemist, as biological phenomena, both physiological and pathological, are, and always will be, extremely complex.

However, when the experimentalist tries to go further in the investigation of the symptoms; when he is careful in determining the cir-

cumstances of his experiment; when, first of all, he avoids creating symptoms which he will afterwards falsely ascribe to the disease; when he does not study the latter thorough the deformation occasioned by therapeutics; when he does everything he can to be a good medical experimentalist, he will have a justified claim on both practitioners' and patients' gratitude; and sceptics will no longer be able to say: take this medicine while it still cures! Well studied, well experimented, the medicine that has cured once should always cure.

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## HUMAN READJUSTMENT OR COORDINATION OF STRUCTURE AND FUNCTION IN THE ORGANISM AS A WHOLE

An Appeal for the Employment or Principles which Guide Orthopedic Surgeons and are of Equal Value for Internists

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The reestablishment of health involves much more than the use of any scheme of medication, dietetics, suggestion, or of any other single means of remediation. When one group of major needs is supplied, if often happens that the organism can and does then recover equilibrium. When, however, this happy consummation does ensue, the problem is shown to have been a simple one; the chief handicap having been removed, the urgent requirements were met and recovery followed.

Man is a vitalized mechanism endowed with rare and varied self-regulative energies, defense reactions, powers for self-adjustment, to meet the needs of admirably designed, elaborated, and balanced structures. The majority of disorders require for their radical reestablishment that adequate attention be given to many accessory, collateral, or subsidiary disabilities or maladjustments, otherwise dissatisfaction may ensue.

Guided reintegration is thereupon needed, an intelligent bringing to a focus and putting to use all factors of remediation in order to achieve a relative norm of vigor, and of balanced consciousness.

Disorder or disease is in no single instance alone; it is always complex. Whatever anomalous states, latent weaknesses, or development faults exist, they must be reckoned with in the accounting.

We must first learn to appraise conditions as they are and the due proportion between primary and acquired defects. The effects of disorder or disease, of acquired inadequacies, of minor deformations, of anomalies in structure, in reflex circuits, of ancient "insults," form a complex group of problems. Many of these are due to wrong habits, omissions, commissions, and commotions. Some or other such handicaps are invariably present in varying form or degree—but there they are, and to ignore any significant one of them is to invite disappointment, delay or defeat. These effects of previous disturbances—notably the less obvious ones—deserve more attention than they get, from the standpoint of readjustments of structure, of function, and also of consciousness. To omit a full, practical evaluation of these residua, whether obvious or determinable or rationally inferable, often nullifies our best laid plans. Hence attention is here asked to certain principles gleaned from the orthopedic surgeons. These when viewed in their due proportions should meet acceptance from every form of medical adviser, especially that most useful of men, the general practitioner.

*Terminology.*—Let me ask consideration for a few descriptive terms which should aid in simplifying concepts so soon as they become familiar. We must come to agreement on definitions which define, and words which describe and do not divert concepts.

I would use to describe the process of straightening out, or adjustment, the word "orthos" or upright—now a part of the word "orthopedic"—and substitute for "pedic" the word "kinetic," or the transition of energy potential into energy kinetic—energy in action, doing, performing, that is, actual movement. Hence we may use the term "orthokinetic," restoring orderliness through one or other of the modalities of movement. These manifestations of movement, active or passive, in their infinite modalities, constitute the prime condition of

livingness. The crux of reestablishment is to stabilize consciousness through conditioned or trained reflexes.

Two forms of consciousness exist, the cerebral and the cellular. With cerebral consciousness we are all very much at home, thanks to the prodigalities of the psychologists. With cellular consciousness we need especially to familiarize ourselves. It is not only on a full parity with the other, but all signs point toward a consciousness which resides in cells, structures, mechanisms, as being rich with undeveloped possibilities in every day exigencies. Orthopedic surgeons during the war have come to accept the imperative demand for greater conscious, purposive self direction of motor mechanisms—assisted volition—in the restoration of many wounds of joints, amputations, and from the start. Here we have mass demonstration of cellular consciousness in the functioning, doing, performing, employed in the work of rescue, restitution *ab initio* and without ceasing. This is kinesia (doing) as contrasted with akinesia (not doing) or rest.

A term is in use by the French, "bio-kinetic treatment," the adjustment of life (bion) through movements of the body (kinesis).*

*The Objectives and Principles of Orthopedics or Orthokinetics.*—Orthopedic procedures aim at the restoration of departures from the anatomical norm, including shape, conformation, posture, and functional correlationships (or adjustments) making for equipoise, symmetry, and harmonious movement. They are applicable equally to a large proportion of clinical or so-called medical or internal problems, and in particular where the element of mechanical disarrangement is prominent, or recognized as causative or contributory.

The problem becomes one of how to recognize and appraise the significance of the factors which produce such distresses as can be removed by readjustment (orthokinetics). The objective is to replace structures which may be found in position of *disadvantage* (thereby inducing the disability) into those of *advantage*. For example: Note the paramount significance of the reciprocal action and reaction of the overlying structures and the organs or viscera they enfold and protect; (1) the chest which contains the lungs, heart, and primary vessels; (2) the trunk and pelvis, containing the digestive, elaborative, and procreative organs; (3) the big muscle masses, static, locomotive, and shoulder girdle as oxygen elaborators; and (4) the accessory and sup-

*In this connection it may be interesting to mention a yet longer but eminently descriptive word to visualize the whole round of bringing about orderliness, suggested to me by Dr. R. Tunstall Taylor, "orthobiokenetics." This may well describe the reestablishment of orderliness in the whole cycle of life processes.

plemental action and reaction of these upon the well being of the special sense organs, the brain and the organism as a whole.

This repositioning includes the means of relieving the disability or even of reestablishing the organism in its entirety.

A review of disadvantageous attitudes, both structural and functional, motor or static correlationships, will reveal the baneful resultants of long antecedent structural anomalies or functional disorders which have produced the element of stress. Among these are: undue or protracted pulls or twists or compressions on muscles, on fibrous structures, on tendon sheaths, on nerves, on venous and lymph channel, also interferences with the economic distribution of static forces whereby disordered, over-tense, relaxed or painful states are brought about, such as follow disturbances in the nicety of poise. The reflexes being disordered (shown by tonic spasm, cramp, or anomalous attitudes of structures), the expenditure of motor forces becomes so large as to stimulate protracted weariness, fatigue. Hence arise tonic spasms, aches, transferred pains, often lameness. These may, and constantly do, produce in acute conditions added distresses which, not being recognized, become merged into the clinical picture already formed, as merely a part of the original or more obvious disability.

Contributing factors to be considered are: protracted weariness, fatigue, or stress passing on to strain, exhaustion or functional commotion. These may arise long before the element of pathogenicity brings about changes in structure, which may be regarded as pathologic.

Among earlier or temporary changes readily observable are: tonic protective muscle spasm, depletion or misdirection of forces being expended through loss of the automatic adjustabilities of the reflexes. The action of a disturbed reflex is shown in both passive and active phases. There is also the negative phase during which the mechanism is in repose and ready to perform. During this negative or resting phase the creature is, of course, not conscious of the reflex tonus. Whenever something arouses a hypersensitive reflex, howsoever little, the active phase is set in motion, keeps it too busy, force becomes expended overactively. This stress, if not relieved, brings about an energy leak. This energy leak leads to weariness, to further stress and, when protracted sufficiently, to strain and finally to exhaustion, also serious perturbation of body or mind. Hence we have not only somatopathies but psychopathies of cognate significances.

Sensory mechanisms become likewise involved, first to so slight a degree as to be only subconsciously recognized as vague distress. Ultimately this distress rises above the threshold of consciousness and becomes pain. Also latent susceptibilities in the reflexes are to be

reckoned with which no doubt vary in different individuals and also in the same individual under differing states or exigencies, but which impair harmonies of function.

Motor and sensory susceptibilities, or variants in susceptibility, serve as the background of disorders called functional. Also there must be considered divergencies in the status or tonus of the regulative mechanisms, the ductless glands, which through hyper or hypo-functioning lead to exhaustion and deteriorative states. Take for example the phenomena of the asthenias, the effects chiefly of adrenal hypofunction, also the well known effects of mild secondary hypothyroidism in producing asthenic states. Indeed, in order to interpret rightly many of the underlying or background states requiring orthopedic (or orthokinetic) readjustment, it is necessary to be familiar with, or consult an expert in, hemadenology (or endocrinology). A familiar example of this defective bone growth, incompetence in ligament, tendon, etc., (hypothymus or hypopituitary), noticeable in such disabilities as weak foot arches.

Consideration must be taken of the fact that disordered states often fail to respond to perfectly correct attempts at orthokinetic (readjustive or orthopedic) relief, for the reason that equilibrium in circulatory and reflex arcs is temporarily impaired. For example: In headache which is capable of being caused by so varied a group of origins, each an acute or subacute state, remedial pressure, such as manipulations made over the posterior occipital nerves, often fails to soothe as it ordinarily does; it may indeed aggravate. So also of backache due to most divertified causes, direct and collateral.*

It should be noted that in order to do justice to the resources of orthokinetics (or orthopedics) in diagnosis or treatment, a fair familiarity must be had with many unfamiliar sources of gross functional disequilibrium. Next we should consider in connection with reflex regulation the various cycles of energizing, the cardiovascular-renal system and its regulation,† the respiratory, the genito-urinary, the digestive and metabolic (peristalsis being the chief motor factor); the special senses (in which reflexopathies are often paramount), and last, but not least, the finer, as well as the gross, motor mechanisms.

Note the effect of an unrealized, often unremembered, over-sudden

*See article by author, "Backache or Tenderness," Int. Clinics, Vol. 1. Series 29, 1919. Also "Fibromyositis," Medicial Record, June 28, 1919. Also reproduced in the Lancet, Nov. 29, 1919.

†See article by author, "Cardiovascular-Renal Regulation, Remarks on Certain Practical Devices or Processes Useful for Conservation and Reconstruction of Cardiopathic Patients," *Boston Medical and Surgical Journal*, October 9, 1919.

action of muscles, in causing agonizing pains. Example: an individual who is muscularly powerful, but long has been sedentary, slips on the ice, automatically makes an immense effort to recover balance, succeeds, then for two or three days suffers excruciating pains due to fibromyositic strain, but the disorder is suspected of being something quite different. So of any extraordinary or unusual muscular efforts. The alarm is often quite pathetic, almost ridiculous, yet eminently real. Almost any form of trauma, displacement, "subluxation," etc., may be incriminated.

To be kept in mind too are the manifold effects of slight arthritides, irritations, often merely metabolic, affecting the joints of the backbone, the rib insertions, and the arthroses, amphiarthroses, and other articulations. Spondylitis has been shown by Vanderhoof (of Richmond, Va.) to be a relatively frequent but a rarely recognized source of much confusion.

Then I may mention the large and varied factor of posture (attitude) faults. Self-acquired or posture deformations may be visualized as due to such compensatory adaptations as the body is impelled to make by reason of effects (chiefly sensory) of protracted irritation whereby functional equipoise in static as well as motor mechanisms is disturbed. They may also ensue upon traumata of less or more severity. All these practically constitute "medical orthopedics" or orthokinetics.

Post-traumatic or post-operative orthopedics (or orthokinetics) is another matter; differing both as to kind and degree. A large proportion of these lamenesses or deformations arising primarily in self-acquired minor traumata or distortions or disfigurements may be so mild as to be scarcely noticeable and only to be demonstrated by expert observation or palpation. Many require little more than replacement by passive (manual) or by actively directed effort or movement remedies (kinesitherapy). Few conditions, comparatively, need severing of tissues (surgical interference), or complete fixation, or immobilization by apparatus.†

Moreover many, indeed a large proportion of lamenesses, disabilities, or deformations are due to tonic spasm, to local exhaustion, to disturbed sensory reactions, to pain reflexes, and disappear upon kinesigenic regulation of activities, especially after localized rest (akinesia), or by suggestion, voluntary relaxation by precise direction, by regula-

†Todd, Clinical Lectures on Paralysis, quoted by Kouindjy; and also Kouindjy, Pierre, "Le Traitement Hemiplégique," etc., *Arch Neurologique*, 1909; Gilles de la Tourette, *Iconog. de la Salpêtrière*, 1897; also Kouindjy and Stragness, "Physiotherapy," C. V. Moseby & Co., St Louis.

tion of "nervousness" (psychomotor or anxiety hypertension), by tactful guidance, by subtlety, such as diversion of attention, and by substitution of energies. Hence the mind equally demands adjustment, compensatory and regulatory procedures, mental readjustment (or psycho-orthokinetics). To secure the mind and body (psychophysical) equipoise necessary it is my experience that soothing touches, tactile suggestions, or deep firm pressures are needed to supplement any mental suggestions; usually both are required.

As to that field to which we might apply the term "medical orthopedia" (Dubois), or let us say, medical orthokinesia, the straightening out of function by means of medication, drugs, biologic or serogenic remedies, vaccines, serums, etc., the subject is so large as to embrace the whole domain of internal medicine and its abundant resources. It is here merely referred to.*

Body defenses are to be studied in accord with the status of reality, of the individual as he is found; that is, his original, acquired, depleted, or deteriorated reactions. My personal inclinations are toward determining how body defects may be set in order from a mechanistic standpoint. It matters less how these deformations or maladjustments have been acquired, and what their extent may be, than it does as to their forms and manifestations and relievability. Hence the nutritive status always looms large and demands primary attention. Each clinician has his "flair," his point of view, his plan of remediation.

All roads, however, lead to Rome—the one goal being constitutional rehabilitation, restitution to the norm, or a relative norm. Through special studies of the ductless glands, the internal secretions, as a pupil of Sajous, I find many problems yield by using the light shed by a study of these great autoregulative governors. These glandular functions are capable of partial regulation by means of the several forms of orthopedia (orthokinetics).

Man, after all said and done, is a sentient mechanism with immense powers of automatic adjustment, of tending to return spontaneously to equilibrium. Man is exceedingly sensitive, yet capable of large self-regulation, and to a great extent, of self-repair, whenever favorable conditions are supplied. None the less is he a mass of static, mobile, interacting motor and psychomotor mechanisms, among which are: framework, muscles, connective tissue, ligaments, joints, tubes, fluids, containers, pumps, distributing channels, reflexes, bellows, gases, cells, reservoirs and regulators of energy.

*See article by author, "Supplemental Action in Reparative Measures, with Special Reference to Serogenic Remedies Reinforced Through Kinetogenic Agencies," *N. Y. Med. Jour.*, Sept. 18, 1920.

Man being a sentient mechanism we must always reckon practically with the status of the "spirit," the mind, the psyche. When the psychogenic status is pretty well grasped, gauged, and the internal processes, biochemical, nutritive, and respiratory, are fairly assessed, it seems to me we are only then in a position to give equal attention to the makeup as a whole. Here the body as an engine for the generation and the transmission, transformation, application and elaboration of forces, deserves equal attention.

No more convenient or practical basis exists on which to appraise a clinical problem than by determining the question whether an individual is adequately "engined" or endowed with energy, also whether he be over- or under-engined—supplied with available power to run smoothly under normal and also under varied, trying, or disadvantageous conditions. Hence the topic of "Types of Men" is interesting in this connection.*

It is not safe to infer that an individual is equipped with just enough vigor to meet most exigencies. Perils ensue from disregarding the dangers of over-energizing (hyperdynamics) quite as much as from low energy content. The "human dynamo" exhibits excess pressure which is a defect of the structures against which pressure is exerted, they being inadequate to equalize the internal pressure. Here we have the analogue of hyper-functioning of the ductless glands.

Military experiences have enriched us here in many directions, none more so than as to the nature, phenomena, and complex causation of shock. From this period we shall do well to appreciate the importance of appraising the shock value. This shock coefficient, reduced to simplest terms, is the capability of recovering functional equilibrium after stresses and strains, and is a province of medical orthopedics, or orthobiotics or orthokinetics.

Surgeons having experience in the war zone tell us that the treatment of all injuries comes practically within the strict interpretation of orthopedic remediation. The attention bestowed on the wounded or shocked (or cell commotioned) requires from the first special care in replacing the injured parts in the most favorable attitudes for advantageous mechanistics for functionation and equilibration, and in immobilization during the jars and jolts of transit and often after reaching the base hospital. Then throughout the treatment adjustment, adaptation, and compensation, also volition, self-direction, are constantly needed, not only to prevent subsequent deformity, but especially

*Stockard suggests that of the over-engined type the majority are hyperthyroid; of the placid, plump, pink type the majority are hypothyroid. This serves as a rough classification.

to defend the integrity of the parts and preserve their functional competence. While rest is one of the chief agencies in preventing, limiting, and curing local infection it must not be unduly prolonged. Voluntary movements are, however, frequently necessary from the outset as in joint injuries. (See the exploits of Willems in conserving joint traumatisms and infections.)

It is desirable that our students of medicine should be given particularzied instruction and training in the principles of orthopedic (orthokinetic) prevention, remediation, and reconstruction. Much progress, so it seems to me, could be made by simplifying, by systematically grouping, all therapeutic agencies and measures. The fact is being made plainer every day that the principles on which these are based interdepend; that they interact helpfully.

We may profitably consider orthokinesis or orthokinetic adjustment and readjustment, as expanded to include the application of orhtopedic principles to most, perhaps to all, problems of human disability, mental as well as structural.

*Psychogenic Factors to be Reckoned With.*—Kinetogenic, orthokinetic, (or orthobiogenetic), principles or enterprises may be visualized under five heads which are interrelated, but not strictly separable, thus:

1. Developmental orthokinetics, primary or constructive kinesitherapy.

2. Mental or psychogenic, or educative, or regulative orthokinetics, the process of achieving conscious control of the body and mind as a unity.

3. Medical orthokinetics, including the selection and application of any or all the resources of internal medicine.

4. Manipulative orthopedia (kinetogenic or coadaptative remediation) by moulding, adapting, adjusting, freeing of limitations, of contractures, of adhesions, also passively moving (mobilization), stretching (traction), directing, in short passive and active hand compulsion within normal limits, etc. In all this the hand is shown to be the one perfect and ever available instrument.

5. Surgical orthopedia (orthokinetics), the use of supports, special apparatus, mechanical guides in action. (The strictly surgical, cutting, reattaching of parts, and the like, will be only referred to and regarded as a separate enterprise; also the removal of offending parts, whatever acts as an irritant or disturber of function.)

All clinical problems involve interactions of the mind and the body, and both require a certain degree of straightening out, readjustment, some more, some less; some by plain and simple means, others are so involved, complex, and obscure as to tax the abilities of the wisest ex-

perts. Also the body needs to be consciously and purposively controlled, to obey the will, and the will (volition, voluntariness) likewise deserves specific or particularized training.

In acute conditions of a trivial or transient nature the mental (psychogenic) element of disarrangement may not be noticeable, yet few persons when out of health escape misconceptions of their personal attitude toward their disorder. Any suffering one is better for counsel, suggestion, explanation, in order to be shown one's duty in its economic aspects, which is mental orthopedia or orthokinesia.

When any disorder becomes protracted or runs into chronicity the need for moral, mental or psychic, and kinetic orthopedia becomes urgent. Hence in a large group of morbid conditions five angles of approach or repair deserve attention, the developmental, the mental, the medical, the manipulative, and the surgical.

If the meager outline here offered does not interest the reader now, it should do so when the lessons of the war come to be better appreciated. Civilian and industrial injuries run each year into the millions deserving similar attention. Moreover the time—by all indications—has come when attention should turn in accord with my aims and those of better men who have taught along similar lines. Out of all the efforts made should emerge *an improved system of therapeutics* in which each and every reputable remedial and curative agency deserves a proportional degree of open-minded attention. The teachings of medical schools must take into full consideration the domain of biokinetics in fitting young graduates to become better surgeon-physicians.

In lecturing, my personal endeavor has been to supply hints and recommendations which shall afford the most good with the least elaborate equipment. Only passing reference is made to those specialized domains of therapeutics such as electrotherapeutics, balneotherapeutics, radiotherapeutics, phototherapeutics, etc. They are left to experts in those arts. Attention is confined in teaching (chiefly) to such instrumentalities as any one either possesses or can readily obtain. One specification, or reservation, must be mentioned, somewhat rare and yet capable of attainment by effort and training. This is:

No one can either diagnose, or successfully treat, a case by externally applied measures who has not a fair equipment in, or knowledge, or appreciation of, the principles of physics; who can think in terms of mass, motion, hydraulics, pneumatics, mechanics, resistances, hyper- or hypo-tonus, tactile apperception, ponderability, in short of biophysics (or physicodynamics or orthobiotics).

He must at least cherish a respect for fundamental principles of hygiene based on facts and less on archaic, fragmentary, traditional be-

liefs, or sheer preferential methods. Candid gleanings of a life time have shown me that the "knowledge" *(sic!)* of hygienic principles employed by the majority of the profession is inadequate and vague. At this point the obvious losses which professional potential has suffered can be replaced and supplied by improved methods of readjusting the organism as a whole.

Diagnosis, general and particular, is obviously the first step; especially is it needful to learn and appraise the nature, extent, and form of manifestation of those instrumental causes on which depend the special kinds and degrees of disability or diseases demanding relief. The fact is, the chief obligation of the clinician is to repair the effects, the residua, of antecedent disorder of disease, and the best, often the only, means is by efficient readjustments.

Full clinical histories should, in every case, be secured. In order to proceed systematically and cover the whole purview, I have devised a "Preliminary History Blank, to be Filled Out by the Patient, the Family, or the Family Adviser." This blank is thorough and has been favorably commented on by reviewers and by those to whose criticism it has been submitted in manuscript. From this complete survey any outstanding points which appear should demand special exploration; the trends of evidence and in particular the local states which promise to reveal what it is important to know in order to institute treatment. This "Preliminary History Blank" can be had from the publishers, F. A. Davis Company, Philadelphia, Pa.

A familiarity is always desirable with the major principles of biophysics which, in my opinion, should be presented to the undergraduates with particularized applications to not only normal but abnormal states. Any physician should read over, once in so often, a primer on physics; this is a most enlightening procedure.*

Two courses of action should arise in the adviser's consciousness in times of need: one is to act promptly, guided by sound inferential interpretations: to supply such urgent help as experience suggests, a hit or miss, rule of thumb, rough and ready, but an efficient method, *e. g.*,

*Physics deals with molecular changes of matter. Mechanics deals with the laws of energy and motion. Psychology deals with the facts of consciousness; with classification and generalization of mental phenomena. Geometry deals with spatial facts. Chemistry deals with atomic combinations and mutations; different forms of matter. Physiology deals with processes going to make the equilibrium of organic life. Sociology deals with processes of social life, etc. Biology deals with the properties of matter and energy of living matter. The lines of demarkation between them are not defined; they interact. The admirable treatise on "Medicial Physics," by John W. Draper, H. C. Lea & Sons, 1886, affords much help. This deserves to be revised and amplified to meet modern requirements.

to fix a watch we may listen to it, note disorders in action, may proceed to oil it, move its hands, shake it, and perhaps it will go. The second and more certain (or orthokinetic) method is to secure particularized information as to abnormal conditions and proceed to readjust them: in the matter of the watch, *e. g.*, to open it and after carefully inspecting its mechanisms, to repair precisely what is found to be amiss.

Human reconstruction is the applying to an individual as he or she presents, at any age, or state, or stage, every reputable means obtainable (in particular biokinetic) to bring his or her coefficient of energy to such a degree of perfection as shall suffice either to: (*a*) raise whatsoever repair energies or survival values are available so as to reach as high a plane as the individual is capable of; (*b*) encourage and enhance the functional powers of all direct and contributory mechanisms in order that the organism as a whole shall respond as completely as possible to whatsoever corrective stimuli, or remediation, may be determined as essential. In brief, the major problem is to do the best for the *man affected by the disease,* and not confine attention to the *disease which has affected the man.*

The first steps are: a searching for, collecting, correlating, combining, and applying systematically and consistently any or all those agencies inclusive under hygiene, and in interpreting them in terms of development or structural and functional integrity to deal successfully with conditions of not only those in ordinary health, but also when states of ill health, and in particular the affects of disordered health (or unhealth) coexist.

Reconstructive remedial agencies (orthokinetic) are applied from without (*e. g.* by physical control or regulation) along with full cooperation with those meliorating agencies for psychogenic control (or mental regulation) inclusive under the term regulation of behavior.

The objective should always be plainly to avow and inculcate the need for, and to render the patient expert in, conscious purposive control, or in self-regulation of that kind, and to that degree, which shall meet the largest variety and number of exigencies.

Attention is commended to the curative value of those activities, in or out of health, which functionate on the sensorimotor level of nervous energy, as contrasted with those acting more prominently on the vegetative (or physicochemical) level on the one hand, and on the other the psychogenic or symbolic level. The proposition includes a summary of all these items and also that comman denominator, a working knowledge of the unit of structure, the reflex circuits or activities, which are capable of affording much assistance in diagnosis, as well as indications and means of treatment.

In the balance of mental (psychomotor) attitude, or poise, or conscious control, there is also to be found the origin of, and key to, the phenomena of tension and overtension, of tonic muscle spasm, hence of exhaustion effects, of contracture, and of referred pains due to strains from maladjustments, wrong posture, static faults, defects in local tone, *e. g.*, excess motion (hypertonus or spasm) or in deficiency (hypotonus or relaxation). Here, among disturbances in this domain or level of nervous energizing, especially when following exhaustion, disorder, damage, or shock, do we encounter a variegated group of body and mind (psychophysical) symptoms whose significance too often escapes right interpretation because wrongly assessed.

The subject of suitable behavior, of self-regulation, of conscious control, taught in accord with expert knowledge of what is right and what is wrong to do, and how and why, I maintain, has as yet by no means received the clinical attention it merits.*

In the absence of expert knowledge of muscle education among physicians the bewildered laity turn to "professors of physical culture," *et id omne genus*, sometimes fortunately and again they fall upon varied forms of error. The regimental drill master does pretty well but he too often is of limited knowledge and crude experiences. The surgeon, especially the orthopedic surgeon, is equipped with much significant information and expertness, but he rarely gives due attention to the correlations of these proficiencies to problems of internal medicine.

As a matter of fact ample opportunity is thus afforded for the exercise of education or training in behavior by expert physicians, especially in restoring health and efficiency to the young men who may be rather below par or not up to standard. In particular is there urgent need for skillful reclamation services, restitution to the full norm, among all classes, groups, planes of society, young or old.

The tendency is to overlook any specialization developed along other lines than one's own, and to be content with our own purview, our range of experience or teaching. Every clinician should have some practical acquaintance with the leading principles of each and every specialty in order to make best selections.

*Mental Readjustment or Reconstruction, (Psychokinetics).*—In every clinical problem the psychogenic or emotogenic factor enters; in some to a greater, in others to a less degree. This is particularly true after long stress and strain and in any protracted state of disability. Hence it is important, indeed necessary, for every surgeon, as well as

*Most physicians would have you believe they are competent to direct in all matters of behavior, of conduct, and even in so simple a one as hygiene, but if you put me on oath I should have difficulty in supporting this view!

physician, to possess some training in conditioned reflexes in psychopathology and psychotherapy.

The point of view here presented is of those conditions wherein mind and body together suffer from the effects of disordered feelings, ideas, and their misinterpretation. The mind is an essential attribute of the organism as a whole. The mental processes in and out of health are usually described from three points of view, viz.: feeling, willing, and doing; yet the whole may be graphically grouped under the will as a name for:

*Behavior is the sum of actions of the body and mind under the control of a personality.* The mind is at all times influential upon the body for better or for worse whenever, or especially wherever, there occur departures from health, from physiogenic and psychogenic poise. This is perhaps less noticeable in acute conditions; but is more pronounced in long standing, protracted or chronic disorders or diseases; also as manifested in their reactive and retroactive effects, direct and indirect. Experience leads to the inference that this department of therapeutics, that of:

*Mind control, direction, conservation, and at times reconstruction* enter as factors of extreme importance in readjusting an ailing person to his or her environment. This environment consists of two parts, that which the individual makes for himself from origins within, and that into which circumstances force him from without. Both of these exert peculiar effects on behavior by producing two kinds of reaction, physical and psycho-physical. The whole demands harmonizing. These psychoreconstructive (psychokinetic) measures then are capable of making over a disorderly mind into an orderly, efficient, reliantly self-directive mind. In the process are evoked the:

*Forces of common sense,* well poised awareness of actual conditions in their normal associations and quantivalences, hope, cheerfulness, wholesome resolves to learn the rules of the game of life, and to play fair with one's self. The object is to induce the patient to see where he has stood in the hierarchy and determine clearly where he now wishes or determines to stand; to realize how essential it is that any problems, arising from departures from spontaneous health, require to be studied with frank cooperation and by guidance of the self-controlling forces and functions all along the interacting nervous levels, the vegetative, the sensorimotor, and the psychogenic.

*Reflexes.*—Closely associated is the subject of the reflexes, reflex circuits the unit or element of nervous function. By eliciting, for example, the reflexes, governing the functions of vegetative life through judiciously applied mechanical stimuli, there is at hand an important

realm of medical as well as diagnostic endeavor. Reflex circuits can be both improved by training and modified or disordered by good or bad habits, and by disease. Some true reflexes can be modified advantageously by attention and conscious control; they may be brought to relative perfection; so also they may be vitiated by a number of somatic disorders and by pathological over-stimulation.

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## THE TEACHING OF MEDICINE AND THERAPEUTICS TO UNDERGRADUATE STUDENTS

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Aside from the increased requirements for entering on the study of medicine, the most noticeable change in medical education in this country within the past quarter of a century, has been the substitution of a large amount of clinical instruction in place of didactic and recitation work. That this has been a decided improvement on the older regime will be admitted by everyone. But that the pendulum has swung too far in the direction of clinical instruction, to the ultimate disadvantage of the student, will be a debatable question. If one visualizes the education of the young physician of a quarter of a century ago, it will be seen that the majority of such graduates stepped out of the medical school into general practice. Unless they were fitted by the instruction of a preceptor, or some practical experience in clinical ward work, such as is given at the present time, they were grossly incompetent. In England, where the system of clinical clerking had its birth, graduates commonly go out into general practice directly after leaving the medical school. The success of this method of clinical clerking in England is generally pointed out when this subject is under discussion.

In this country, however, at the present time an entirely different course is pursued by at least 98 per cent. of the graduates. Throughout the country, it may be said that it is an exception that a student fails to spend a period of at least one year as interne in a hospital. In many instances, two or three years are spent in this way and an abundant practical experience is gained. In view of this clinical experience, is it not germane to ask, whether it would not be better to concentrate the work in the medical school on the book-side of medicine, rather than to have the student spend, as he does in nearly all Class A schools,

between sixty and seventy-five per cent. of his time in the senior year in clinical and ward work? From the standpoint of popularity with the student, there can be no question but that clinical instruction is the most favored form of instruction; he feels that he is learning without effort. In many instances, the clinical teacher likes it better because it is less onerous from a pedagogic standpoint. However, these reasons do not make it clear that clinical instruction is preferable. The objection will be raised that the student has, by the time he enters the senior year, completely covered the principles of medicine. If this were really so, and if he had grasped all of the essentials, there could not be any justifiable argument against the present arrangement, and this brings up the whole question as to the best methods of teaching the practice of medicine. Everyone has met students whose minds were so active and so receptive that, in the first instance, they grasped and retained practically everything given by recitation or by lecture. Such minds are few and far between. Fortunately, or unfortunately, many of these quickly climb the ladder of success and take their places as teachers of medicine. I say, possibly unfortunately, because the possessors of such minds, and they are inherited—not constructed by educational methods —expect the student to have mentalities like unto their own and expect him to grasp and retain all of the mental pabulum offered to him. Extended experience has made me feel that most of the fundamental facts and theories of medicine must be repeatedly driven into the average mind, before it is definitely fixed there. If one goes back and visualizes his own experiences as a medical student, I think that most of you will agree that your first reading or lecture, on any of the great problems in medicine, was mere jargon. This mental indigestion can be easily recognized, particularly in an attempt to study the anatomy and diseases of the nervous system, as well as the irregularities of the heart. This is true, to a greater or less degree, with all of the problems of medicine, but it is not so easily recognized. After going over such a subject a dozen times or more, order begins to grow out of chaos, and the facts become readily accessible to one's memory; even at mature age when one takes up some problem, such as, for instance, irregularities of the heart, mentioned above, it requires many repetitions of the facts before they can (as it were) be placed on one's finger tips. Of course, it is true that one occasionally meets a very clever student who recites brilliantly the first time he has studied a subject and who has this information readily accessible for years afterward, but he is the exception rather than the rule. It is not an uncommon experience in ordinary work, to find that such a student may recite or grasp a subject at the time of demonstration or recitation, and yet in from three to six months,

when the identical question is put, his mind is for the most part a blank. If someone else has taught him this subject before, it may give a sense of satisfaction to the questioner and he, the examiner, may readily be excused if he says that the student was, unfortunately, not properly taught, but if it happens to be one whom he himself has taught, one has an opportunity to *swallow hard* and is not so filled with self approbation. The only practical solution for dealing with ordinary minds is continued repetition. The exponents of clinical instruction, as opposed to text-book instruction, maintain that by the presentation of the actual case, the subject is more firmly impressed upon the student's mind than is the text-book picture of the same. For the vast majority of minds, I do not think that anyone can seriously dispute this claim; on the other hand, each clinical case can represent only one phase of any illness, whereas the text-book picture covers many varieties of the disease. It is a practical impossibility to deal with more than a very few clinical entities in any single session, whereas the text-book recitations cover a large number of clinical pictures; furthermore, no matter how large the service may be, it is a physical impossibility to have any regular systematic sequence of cases. Unless this is done, many facts fall between and are lost. From a pedagogic standpoint, it is generally accepted that memory, certainly available memory, is better acquired when mental impressions are made on as may senses as possible; in other words, a fact that comes to the mind through three senses is more apt to be fixed than one acquired through one sense, so that when one hears a subject discussed, writes the same subject, reads it over and over again, masticates it, digests it, and then puts it forth in the form of a recitation as his own mental product, which it is, he has a better detailed understanding of it, and it is more permanently fixed, than when he simply visualizes it in the shape of a clinical demonstration. It will be objected, that we visualize most of the incidents in life; even if this is granted, we do not visualize them in the sharp details, that we do the well repeated printed page. It must be granted, in any discussion of this subject, that there is no single process of mental fixation that will work for the minds of all students. To some minds, the clinical picture is a fixed and lasting impression; probably this preference depends on inherited racial traits, but for the average student, as I have seen him, I am convinced that book knowledge fixes a more accurate picture in his mind than clinical observation, provided he digests it and puts it forth in the shape of a recitation. Incidentally, I might remark that, in discussing this matter among teachers and practitioners, I have found that the surgeon usually answers, that he considered the clinical teaching

superior to the book work, whereas the medical mind, in most instances, prefers the opposite.

I believe that the student's interest should be stimulated, to some degree, by seeing and looking after some clinical cases, from his second year in medicine, but this should not, as it is doing now, largely eliminate text-book recitation. The phase of the lecturer has justly been replaced in most schools. The number of teachers who can cover the ground by lecture, interestingly, without a clinical case in evidence, are admittedly few, and the text-books are so good and complete, that competition is out of the question, yet there is a field for some lecture work, just as there is a field for clinical instruction. With the passing of the lecturer one finds fewer idols in the shape of the old professor. If the whole subject of Materia Medica and Therapeutics of any text-book, were recited on year after year, there would not be so many practitioners taking up every new medical fad that is brought into their office by the detail man. As it is, dosage is seldom fixed in the student's mind; for that reason, he orders the proprietary, which he knows is not, in a general way, going to be toxic and he does not have to worry over dosage and incompatibility, and it saves him mental calculation. He does not stop to consider that the dosage is likely to be too small for any physiological effect, as long as the label states that the bottle contains drugs that he knows have therapeutic value and which, furthermore, states that they have a specific value for the type of case that he has under consideration. If he has his dosage fixed in his mind and readily available—as available as the months of the year—he is not apt to fall into this habit of allowing someone else to set the dosage. The study of dosage is a steady grind, that must be gone over and over by many frequent repetitions, and not by lecture or any kind of demonstration.

Recently, in a hospital examination of students, from various schools, I asked twenty-five men, what was the dose of fluid extract of Buchu and what was its principal use. It was surprising to find that 50 per cent. had never heard of the drug, some thinking it a patent medicine. If any standard text-book had been studied, and recited on from beginning to end, and repeated at least twice, such ignorance would be impossible. It is, particularly, the minor subjects that are apt to be missed in classes where the text-book is not made paramount. It will be objected that there is a certain amount of material in the text-books that is useless from a practical standpoint; this must be granted, yet any standard text-book covers the subject completely and makes the student familiar with the terms of the subject, so that, even though he forgets much of the total, the subjects and terms are not strangers

to him when he sees or needs them, and at least he knows where to find the facts. These contentions pertain not only to the teaching of diagnosis, but to therapeutics as well. The knowledge of the action of drugs is largely a matter of memory. The experimental pharmacology is necessarily limited and the student must get the knowledge of drugs from many angles, but above all, from his text-books. The attempt to teach *all* therapeutics from a pharmacological standpoint entirely is a failure, and makes for an attitude of mind, that, unless things can be proven, they are useless; in other words, it causes loss of faith, unless positive proof is forthcoming. There are so many things in life that we must take on faith, that cannot be proved, that without it, life would be very uncomfortable. This attitude of mind is a perfectly proper one for the investigator, but it does not fit well in general practice; it is an attitude of mind that, once developed, is difficult to throw off. It is, undoubtedly, a large factor in inducing the medical student to prefer surgery and specialties, since his work can be seen and proven, definitely, without any question of faith or doubt. At the present time, I believe there is too much time spent on "fad lectures" and the minutiae of the specialties, to the disadvantage of the major subjects. Some of this is doubtless due (1) to the frequently repeated lament of the older practitioners, who state that they were never taught such and such in their course; (2) to the enthusiasm of the specialist who thinks that the entire field of medicine revolves about his orb; (3) to the student who thinks he ought to be taught every new method that he reads in the journals and who feels that he could outline a medical course better than the Faculty. As it is, the curriculum is overcrowded in all Class A schools.

In summing up this discussion, we would like to point out that (1) Clinical instruction, in the three or four years of medicine, must constitute a large portion of the instruction of the student in medicine, who does not take a hospital interneship in a properly graded Class A hospital. (2) When a hospital interneship is taken, the time spent in medical school on clinical instruction may, for a *large* portion, be more profitably spent in text-book study, than in ward study. (3) Materia Medica and therapeutics, certainly the latter, are better fixed in the student's mind, in the medical school, by many repetitions of his text-book, than by a physiological demonstration. I am perfectly aware of the fact that the views here expressed will be considered by many as being reactionary; anyone who runs counter to popular movements is thought to be reactionary, yet these views have been crystallized, after fifteen years of teaching, under both the text-book and clinical regimes.

# ON THE AIMS OF INTERNAL THERAPEUTICS*

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Every pharmacological, but no less every physical influence upon the organism represents a sum of stimulations upon the cells of the body. By stimulation we here understand all influences upon the morphological and functional entity made up by the organized cells, whether this action be caused from without or from within—in the latter case from the functioning of the cell itself. A priori it may be said that, in principle, there must be two kinds of stimulations that are of different natures: first, those which are adapted to the chemical and structural organization, which can be termed, *adequate stimulations;* and secondly, those which, owing to their nature, cannot be adapted to the chemical and structural organization—*inadequate stimulations.* A cell can react upon a stimulus only when the latter corresponds to the cell's organization, which again is given by the constitution of the macroorganism. For the cell of the intestinal epithelium the molecule of the glucoside of digitalis constitutes no stimulus while it does constitute one for the heart muscle. Just as little can a morphine molecule effect an influence on the cell of the bone marrow. In the sense of a general external reaction these bodies are indeed stimulations, but the above cell species, by their very constitution, have no possibility of reacting to this stimulus in a manner typical of them. Their "immanent" specificity has no effective relation to an inadequate stimulation. Such a behavior has been known for a long time in the doctrine of immunity which is explainable by the deficiency of receptors. Accordingly a cell responds upon adequate stimulation only, and then in a specific manner. The law of specific energy of the sense organs has an analogue in the specific irritability of each single cell organism.

Physiologically the cell experiences stimulations only from its own healthy macroorganism, and these are always adequate since they represent on their side functions of personal identical cells or cell groups and therefore arise from the identical general constitution. A renal cell reacts with its specific function, diuresis, only in response to an adequate stimulus. If it were possible to transmit to it a stimulus which would, for example, contract the trapezius muscle, no diuresis could be expected. It would not be adapted to the renal cell and its specific activity. The adequacy involves both a qualitative and a quantitative moment; accordingly there exists adequate physiological and unphysiological stimulation. To this group belongs the electrical

*Read by invitation.

stimulation which can produce a specific reaction in the renal cell as well as in the muscle cell, but does not occur as a purely electrical stimulus in the physiological working of the body. The electrical stimulus must by no means be identified with the mere processes of conduction in nerves. Chemical and physical processes of different nature play a role not as yet sufficiently investigated, in physiological stimulation.

The classification of possible stimulations may be attempted thus:

A. *Physiological stimuli may be:*

*(a)* endogenous, i.e., they take their origin in personally identical cells.

*(b)* exogenous, i.e., acting only upon cells that are receptively adequate in a special manner, such as resorption cells of the digestive canal, or of the lungs, and sensory cells.

*(c)* always adequate, i.e., they are both qualitatively and quantitatively adjusted specifically to the constitution of the cell that receives the stimulus. This is based upon a common coordinating relation of both factors, namely, the stimulus and the receptive cell.

B. *Unphysiological simuli may be:*

*(a)* endogenous: under pathological conditions cells may be formed, the products of which represent in their diseased and changed original substratum a conditional deviation from the personal normal state (toxins of malignant tumors, etc.).

*(b)* exogenous: of not personally identical origin.

*(c)* adequate: inasmuch as their nature is of such a character that the living substance can react upon them (thermic, chemical, electrical stimulations). Here the cell reacts by virtue of its innate specificity.

*(d)* inadequate: the stimulation in question does not represent any stimulus for the cell. There does not exist any chemical or other relation between the stimulus and the receiving cell.

From this survey it is evident that the purpose of every therapy must be the preservation and increment of the healthy function which is most surely achieved when medicaments are used so that the quanlities of the physiological stimulus are preserved. At all events, the quality of stimulus designated under B *(b)* must be avoided.

All unphysiological stimuli have the common quality that they are more or less easily exhausted. Eventually habituation to the stimulus

sets in which necessitates a continual increase of the stimulus. In the case of employment of some medicaments, even toxic substances in the long run lose their poisonous qualities. The latter may be called only a function of the quantity or of the quantitative intensity of the stimulation; the destructive effect of certain bodies upon the living substance always depends upon a certain minimum. Physiological stimulations, on the contrary, do not lose their effectiveness by the duration of their influence, but only through a general senility of the cells. If physiological stimuli grow ineffective, it means the normal death by age of the organism.

The sphere of lastingly effective interferences, however, is restricted in therapy by the fact that exogenous physiological stimuli presuppose a specifically adapted cell system for the evolution of their effects. The sharply defined functional relation—digitalis, heart muscle; morphine, brain ganglion cell—is not met with in many cases. Often we are dealing with "polytropic" remedies, as in the case of many alkaloids (atropine, etc.). This "regional breadth" of effectiveness, in the special cases often undesirable, is characterized as a secondary effect, which, however, makes the success of the therapeutic effect questionable.

Under this viewpoint a certain therapeutic school which has only lately attracted attention gains in importance. Through the work of Weichhardt and his collaborators the conception of protoplasmic activation created by this investigator was given at least an empirical importance. The meaning of this expression is to be found in the increased power for work of the living cell due to certain therapeutic influences. General increase of the functions of active organic cells at first resulted from the direct introduction of albumin and albuminous disintegration products into the blood stream with exclusion of the intestinal canal. Weichhardt and Schittenhelm began with investigating the immediate effect of such albumin upon the blood picture, metabolism, and especially the thermic centers. The method then became more generally accessible through the investigations of Rudolf Schmidt and his disciples. They used milk injected in doses of 5 to 10 c.c., as their therapeutic agents. The general effects in this procedure were the same as with the injections of muscle "juice" applied by Weichhardt. An increased temperature and neutrophile leucocytosis constitute the general effect. This method was very soon used in therapy. (Grote, proteintherapy in *Zeitschrift für Ärztliche Fortbildung*, 1919, N. 24, where the literature may be found.)

Certain observations upon which, however, we shall not enter, favor the idea that the therapeutically working principle of protein body therapy is to be found in albuminous disintegration products formed by proteolysis in the tissues caused by the proteins that are injected. We

are dealing here with amino acids and similar bodies. But these—and that is of fundamental importance—are not essentially different from the disintegration products normally found in the body. Through this method a possibility seems to be given to inject stimuli into the body-cell that are adequate to it. These stimuli, although provoked exogenously, nevertheless work in exactly the same manner as stimuli that have arisen within the body itself.

Already these experiences have been applied to the known immune therapeutic successes with specific sera, and it might be discussed whether or not the effect of tuberculin might not in the last analysis be due to the action of a mere nonspecific protein disintegration product. R. Schmidt obtained from milk injections the same focal reactions as with original tuberculin. Bingel in Brunswick (Monograph, publ. by F. C. W. Vogel, Leipzig, 1918) treated diphtheria with horse serum free from immune bodies: his successes are as surprising as satisfactory. Typhoid fever has been treated in a similar manner successfully by Saxl and Grote. Especially satisfactory were the successes with male and female gonorrhea and its complications. (R. Müller and Weiss). The well-known undeniable good influence of blood injections on anemias of all kinds very likely is due to the same principle.

The important point in this matter seems to be the fact that in reality in this therapy we exert only a physiological stimulation. The body is in no way offered an agent with which the cell cannot accomplish anything. Albuminous disintegration products constantly circulate in the body and their temporary increase is the medium of stimulation which causes the cell to increase its most proper vital functions. This therapy represents an exogenous adequate stimulation which the body itself through fermentative action changes into an endogenous adequate stimulus, bestowing upon it thereby, according to our division, the character of a physiological stimulation.

With this insight there seems to be established the principle according to which all future medicinal and physical therapy will have to work, namely, *the changing of an exogenous stimulation which is accessible to the ferments of the body and which consequently must be adequate—into an endogenous adequate stimulation for the individual cell.*

A more accurate analysis of some hitherto called specific interferences (e.g. serum therapy of carcinoma by Abderhalden, etc.) will very probably show that the same principle is at the bottom. At any rate, the so-called "immune bodies," known hitherto, are not identical with the substances effective in protein body therapy. They may cooperate, but their role is only a secondary one, since it appears possible to increase them, or at least to activate them by the physiological stimuli.

It will be the task of future investigation to test the individual disintegration products as to their effectiveness in increasing cell work or cell resistance. Even now it seems certain that not all bodies formed in the fermentative parenteral splitting process are of equal value as to their effect upon the cells.

In the foregoing deduction I have considered also the physical actions. This was done because in physical influences (heat, cold, electricity, Röntgen rays, etc.) similar fermentative splitting processes of protein (protein disintegration) can be presupposed as parenterally originated in the body. But the details are totally unknown as yet. It has been possible, however, to demonstrate such processes in the case of extensive burns.

But this will not put an end to the specific immune body therapy. It means rather a clearer comprehension of its possibilities and purposes. The specific antitoxin, *e. g.* of diphtheria serum, fully retains the significance which is given by its specific binding to the bacterium. But there is the possibility of an essentially increased effectiveness as soon as we shall know the means by which we may assist the living cell of the organism in the functions injured by the infection. That the diphtheria antitoxin itself cannot do. It is specifically adjusted to the bacterium (Klebs-Löffler bacillus). The bacterium, however, is not the essence of the infectious disease. The essence is rather found in the lowered function of the cells in the body. Therapy directed by these viewpoints, *i.e.* the highest possible conservation of physiological stimuli for the purpose of greatest possible preservation and strengthening of physiological function, will be in the best sense a therapy that can be termed etiological.

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## SOME OBSERVATIONS ON THERAPEUTIC NIHILISM

By F. M. POTTENGER, A.M., M.D., LL.D., F.A.C.P.
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During the past thirty years a revolution has been going on within the ranks of medicine. Coincident with the development of laboratory methods and the discovery of the causes of many diseases prevention assumed the place of first importance while the cure of disease and the relief of the patient's symptoms took a secondary place. With this relegation of the practice of medicine to a place of secondary importance has come a change in the relationship between physician and patient. The old family physician with his medicine case full of pills and his heart full of interest in the patient and sympathy for him in his illness has been almost pushed off

of the stage by the man whose chief interest lies in the study of diseases as they appear through the microscope, and in the test tube, and whose thought of the patient afflicted has necessarily appeared to be minimized.

Both the profession and the public have recognized and deplored this change with its inevitable result of separation of interests. The sick man demands more than our scientific medicine is giving him. He requires more than a knowledge of disease and disease processes can furnish. Nor is his illness confined to his material body alone. His condition as a thinking, willing, hoping being is also disturbed. One of medicine's great mistakes has been its failure to recognize that there are two factors to be considered, the patient and the disease; and to give to each the consideration which it deserves. It has pursued its studies and its practice with a lack of comprehension of the nervous and psychic sides of the individual, and a failure to understand his reactions toward disease that seems inexplicable.

The older medicine without the knowledge of the causes of disease and of pathological changes in the tissues caused by them, which we possess today, failed to satisfy the investigating mind of medical men, but it gave much comfort and satisfaction to the patient, because it made him the center of interest. Modern medicine with its development of the various laboratory branches and specialties has taken upon itself a far more scientific aspect than the medicine of previous times, which has been a great source of satisfaction to the profession; but can we claim that it is appreciated by the layman to the extent that our belief in its superiority warrants? If not, why not? The answer is very complex, but I desire to point out a few facts that I believe are fundamental to its understanding.

The age through which we are now passing has been dominated by bacteriology and pathological anatomy. It has been an age in which the study of material factors has received greater attention than nervous and psychic. Pathologists, too often, have been out of harmony with the efforts to treat the sick, and too often, with an air of superior knowledge rather than an air of helpful suggestion, have shown at the post-mortem table the errors of the clinician's diagnosis. They, too, with dogmatic assertion have announced that therapy can not change the pathology of disease. Those who have been best informed in pathology have often been most pessimistic as to the accomplishments of clinical medicine in both diagnosis and therapy. Unfortunately this pessimism on the part of the more scientifically trained toward the practical application of discovered facts to the relief of symptoms and cure of disease has led to the study of the problems of each branch of laboratory medicine as a specialty with insufficient thought to its application to the practice of medicine.

It has also made the path of those who practise medicine unnecessarily difficult.

Aside from this group of ultra scientific men there have been those who have been obliged to minister to the sick and help those who are ill to overcome their disease. They have not always measured up to the height of scientific standards in their work. Thy have had a hard time to square their accomplishments with their own ideals; but they deserve honor to the extent to which they have added to the sum of medical knowledge and succeeded in applying it to the relief of those who are ill. Some practitioners of medicine have assumed a disinterested attitude toward the laboratory side of medicine which is comparable to that of the many laboratory workers toward medical practice. This is illustrated by the following incident. A physician was doing post-graduate work in Vienna. Some of his colleagues were telling of the wonderful opportunities for study under Prof. Weichselbaum and his assistants in the Pathologic Institute and invited him to go with them. He replied "Weichselbaum never cured anybody." This practitioner, who only wanted that which would aid or cure his patient, and the pathologist, who laughs at the errors in diagnosis and ridicules the attempts at curing disease, represent the extremes in medicine. The one's opinion reflects the pessimism which comes from an appreciation of the paucity of our real knowledge and a lack of sympathy for the problems of administering to the needs of the sick; the other shows a failure to recognize the importance of a study which does not directly aid one in his desire to meet the demands which are made upon him to do something to relieve his patients.

The main error on the part of the pathologist is that he assumes too much for his branch. He has assumed a place of much greater relative importance for pathological anatomy than time will accord it, after the correlated branches of medicine have been thoroughly developed. No one ever will be accused of knowing too much pathological anatomy, but the error is in measuring its importance in relation to medicine as a whole. The error on the part of the practitioner is that he recognizes the problems of the practice of medicine but fails to see that the knowledge derived from the study of these laboratory branches is essential to the unfolding of the science of medicine, and that the greater medicine can come only through correlating the knowledge derived from study in all of its branches.

Physiology is one of the most important studies in medicine. Normal physiology contrasted with pathological physiology, gives our disease pictures and furnishes data upon which to make a diagnosis and establish a therapy. Further, physiological action is subject to change

through therapy. Even pathological anatomical changes in tissues are sometimes brought about by altering physiological function and are relieved by correcting it. The study of pathological anatomy, although not intentionally nor necessarily, has fostered medical pessimism and the spirit of therapeutic nihilism; the development of pathological physiology, on the other hand, will bring a clearer conception of the working of the human machine in health and disease and will add intelligence and optimism to diagnosis and therapy.

The development of diagnosis and therapeutics will be greatly aided, if our profession can only obtain a broader grasp of what medicine is. Medicine is a comprehensive study of the causes of disease; the prevention of disease; the effects of disease upon the body tissues; the manner in which functions of the body are disturbed by its presence; the nervous, endocrine and psychic imbalance which is brought about by it; and measures for the cure of the patient or the relief of attending symptoms.

Each branch, whether it be pathological anatomy, bacteriology, biochemistry, physiology, pathological psysiology, psychopathology, or any other, is only a part of medicine. One branch may be of greater importance than others in the minds of the profession at one time and in the minds of some members all of the time; but one must never lose sight of the fact that they are one and all only of interest to medicine as they can furnish information which helps to prevent or cure disease, relieve symptoms, or alleviate suffering.

Therapy will be a legitimate and necessary branch of medicine as long as illness exists. No pessimism can destroy its usefulness and no nihilistic attitude can remove its necessity. If therapy is a necessity, then it is the duty of medicine to develop those phases of study which will make it more accurate and more successful.

No one can read medicine without recognizing the force of the struggle for better therapeutic measures. This struggle, however, has not been guided by a clear conception. Much of the effort in the past has been confined to the discovery of plants with medicinal virtues and chemicals which would in some way relieve symptoms. There has been too much of a tendency to confine ourselves to drugs and surgery to the exclusion of physical and psychical measures.

This grasp of therapy has been wrong. While theoretically our profession stands ready to employ any measure that will aid in the cure or relief of disease, in practice we have been extremely narrow in our attitude toward remedial measures. Probably the majority of graduates from medical schools in the past have left college with the idea too strongly in their minds that disease was to be cured, if at all, by drugs

or surgery. The fact is that they have graduated without a true conception of what the practice of medicine means.

It is no wonder that medicine has found itself so vulnerable to the attacks of isms and cults which have arisen during recent times; for in its own ranks it has many who scoff at therapeutic attempts. The purely scientific worker, often possessed of the best brains of the profession, rarely interests himself in therapy and is too often content with the statement that drugs influence disease processes but little, if any; and the surgeon, carried away by his brilliant advances in his field and not yet fully appreciating the shortcomings of his therapeutic attempts, is too much of the opinion, "surgery or nothing." On the other hand, there are many practitioners who from their intimate contact with the sick, make an earnest effort to find methods for relieving symptoms and cutting short the period of illness. The more eminent the man the less he depends upon drugs and the more he prescribe's proper care and regulation of the patient's life. The physician with less knowledge and reputation, however, is apt to depend mostly upon drugs for his results.

Medical teaching fails utterly in preparing men for meeting the thrapeutic demands made upon them in practice. The graduate in medicine is imbued not so much with trying to help the patient as with trying to understand his pathology, bacteriology, and pathological chemistry. The patient on the other hand desires relief from his symptoms, and has no interest in the recognized scientific line of study unless they give him relief.

While some disease processes have anatomical changes standing as causative, others have them only as a result. All, however, show physiological change resulting in disturbances in normal function. It is the duty of physicians then, to study thoroughly normal and pathological physiology, to learn what governs the normal working of the human organism, and to recognize the manner in which disease alters this. This leads to a thorough study of the nervous, endocrine, and psychic controls of the body with the application of remedies and measures which will preserve or restore their balance when disturbed.

In a former paper, in discussing this point, I called attention to the fact that normal physiological action is under the control of the nervous and endocrine systems and that during disease these systems are disturbed by stimuli which are of either physical or psychic origin. It seems to me that this covers comprehensively the control of body action in health and in disease.

It is the duty of medicine to comprehend these controls fully and also to learn the things which will restore them to normal when altered. Drug therapy is based on the action of substances, upon nerve and

chemical control. To the extent that we learn the physiological action of drugs shall we be able to use them with intelligence. One would think from the teachings of materia medica that the principal way of influencing disease is by drugs, but in practice such is not the case. Any measure that may be employed to remove or directly combat the cause of disease or to counteract the pathological action of any organ or tissue may be utilized in the treatment of disease; so may any measure that will increase the normal stability of the nervous and endocrine systems and improve the physical and psychic condition of the patient so that he will better withstand the disease.

The treatment of the sick then is accomplished in three principal ways: one by attempting to remove that which is causing the disease, another by restoring disturbed function, and a third by attempting to stabilize the nervous and psychic equilibrium and aid the organism in making its own fight to overcome disease. The first has been considered the most scientific during recent years, but because of the limited headway that it has made, it has caused great discouragement to practitioners of medicine. The other methods, while not having as yet fully gained the recognition of scientific men, have been gradually gaining in general favor. Practitioners are beginning to see that anything which will aid the sick is worthy of our profession, and that it is necessary to continue aiding the patient in whatever way we can even if specific remedies cannot be had and the cause of the disease cannot be surgically removed.

As we turn to this rational view of medicine, it brings with it a demand for a closer study of the patient than we have heretofore given him, and a better understanding of his normal and pathological reactions. At the same time it offers a hope for the displacement of pessimism and nihilism in therapeutics and the establishment of a basis upon which medicine can render a more efficient service.

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## THE FUTURE OF THERAPEUTICS

By REYNOLD WEBB WILCOX, M.D., F.A.C.P.,
New York

Twenty-one years ago last month this Society was organized under the presidency of Professor Horatio C. Wood in this city. According to the critics this Society was entirely superfluous because, in those days of the full flower of therapeutic nihilism, therapeutics was as nonexistent as is disease in the concept of the blind devotees of a contem-

poraneous cult. But the founders of this organization, men of deeds and with prophetic vision, realized that the theories of the nihilists were incompatible with the proper fulfillment of the duties and obligations of conscientious practitioners of the art of healing. They realized that a thorough knowledge of pathology was essential and that diagnosis was important, and equally well that the period which should elapse before the necropsy should confirm or modify the diagnosis ought not to be one of watchful waiting if the duty of the physician to the patient was to be properly appreciated and fulfilled. In other words, an idle observation of the combat of the human organism against infection or the the progress of degenerations of important organs or the impairment of functions, no matter how interesting these might be, was not the sum total of the professional activities of the attendant. Indeed, this inactivity, considered in the light of results, differed little from the beating of tom-toms of the aborigines or its modern successors, the reading of congeries of words, meaningless, irrelevant, immaterial, and incompetent in the presence of a real tragedy.

Slowly but surely the profession has come to realize that he who proclaims that there is no treatment of disease simply asserts that that particular individual knows no treatment and the term therapeutic nihilist has become coterminous with that of therapeutic ignoramus. Further the contemplation of the end results of disease and the study of the havoc wrought by morbid processes, as carried out in the dead house, beget a feeling of pessimism as to the effectiveness of methods and means employed to combat disease. And as it began to be realized that the ruins of the fireworks on the morning of the fifth of July gave little ground for an estimate of the oratory, the enthusiasm, and the more deeply grounding of patriotic sentiments and founding of nobler aspirations of the preceding day, so the despair of the pathologist became out of place in the clinician who knew his resources, as well as their limitations, in alleviating suffering and in the cure of diseases. Hence the cheerfulness of the expert and the hopefulness of the conscientious practitioner made for a more favorable prognosis not only for the patient but as well for scientific knowledge. What has been said applies not only to the domain of internal medicine, for it is here that a real cure, a *restitutio in integrum*, is the goal more frequently reached, but to surgery also, although that often is a process of subtraction, and to the limited specialties. So this Society, early in its history has enrolled in its membership representatives of all departments of professional activity to the advancement not only of group therapeutics but also of therapeutics in its broadest meaning which has been the outstanding purpose of this organization. If we had accomplished nothing

more than this the *raison d'etre* of our Society would have been amply justified by the results.

But our achievements have not been limited to the general acceptance of the fact that pathology is not the whole nor even the major part of medicine; we have demonstrated that pharmacology is not all of therapeutics nor even a respectable moiety of the healing art. This Society pointed out in 1903 (Transactions, Vol. II, p. 26) that a necessary basis for the highest development of the art of therapeutics should be: (1) A practical acquaintance with various remedial physical measures and remedies, not less physiological, and methods of preparing the latter. This should be acquired during the early and mnemonic period of the student's career (recitation and demonstration). (2) Actual knowledge of the action of agencies and remedies acquired by personal experimentation and demonstration under the teacher's eye (laboratory demonstration). (3) Application of these agencies and remedies, the actuality of their effects for good or evil having been fixed in the student's mind, in the treatment of diseases and symptoms, under proper supervision lecture and clinical demonstration). (4) The actual direction for the exhibition, in strict pharmacopœial nomenclature, of remedies and the scientific use of physical agencies must be so thoroughly comprehended by the student that he can not only intelligently apply them, but give valid reason for his treatment (clinical practice and conferences). That the schools have not been alive to the importance of this basis for education, thus categorically expressed, is the fact that a *questionnaire* sent out by one of the most important, if not the most important, of the medical schools, to graduates of more than ten years' standing, elicited the information that more than three-quarters of those who reported attributed their failure to obtain their hoped-for success in practice to the imperfect teaching of therapeutics in the school from which they had obtained their degree. That this is not either a local, or an unusual condition is evident from reading a forcible paper which was presented at our last meeting in Philadelphia by Spencer L. Dawes. Further evidence, if such evidence were wanting, is contained in the assertion of the dean of a medical school which for many years has enjoyed the traditions of a faculty of national reputation and a graduate body of successful practitioners of which a respectable number have been of great reputation for ability and professional skill, and remarkable for their loyalty to their *Alma Mater*. This school has recently been reorganized along the lines of emphasis upon the laboratory and preparation for the student's life work largely founded upon generalities of treatment without special emphasis being placed upon an actual knowledge of the materials used in the treatment of dis-

ease and their application to the concrete problem under consideration. This dean in explaining the failure of this new system makes the naive assertion that success in the practice of the healing art depends largely upon the personality of the practitioner, apparently not realizing that the primary and proper function of the medical school is to educate competent physicians and surgeons. In attempting to develop investigators he fails to realize that some potentially succesful practitioners may fail to attain their greatest usefulness because of his system. It would seem that in the classification of medical schools, not only the form of instruction should be determined, but the character of the instruction and the amount of it considered in its proper perspective, that is its bearings upon the equipment of the profession of the future which must take up the work which is now being done by the successful practitioner of the present.

Another set of critics predicted the ownership of this Society, or at least its control, by some enterprising group of manufacturers of materia medica products basing their prophecy upon the history of similar organizations (societies or sections). Article X, Section 3 of the By-Laws reads as follows: "No paper, report, abstract, or other communication either written or verbal, which, directly or indirectly, commends or advertises any secret, patented, or trade-marked products, or method of treatment, shall be presented to, or received by the Society; nor shall any discussion upon such products, or methods, be permitted: Provided that nothing in this section shall be construed as presenting adverse action upon such subjects." This section, rigidly enforced and conscientiously lived up to in the letter and the spirit, has resulted in the disappointment of the prophets of disaster.

As to the Pharmacopœia, this Society has always realized its importance and earnestly advocated that the profession become better acquainted with its resources and employ its open, standardized, and eligible preparations. Many members have taken an active part in the decennial revisions which have been made during the life time of this Society.

The importance of the dissemination of accurate and impartial knowledge of the unofficial remedies was early a subject for discussion and action by this Society, and this finally took concrete form in the National Bureau of Medicines and Foods as was originated and proposed by Francis E. Stewart (Transactions, 1903, Vol. I, p. 62). Later the plan, although not in its entirety, was put into practical operation as the now-known Council on Pharmacy and Chemistry, which has been of great benefit, through the publication of the results of its activities, not necessarily constructive, to all workers in the domain of medicine and surgery (Transactions, 1908, Vol. IV, p. 69).

In constructive work to every department of the science of therapeutics this Society has made fruitful and substantial contributions. Every volume of the Transactions has recorded marked progress in the underlying sciences which has markedly improved the practice of therapeutics in its broadest sense. The value of therapeutics is now unquestioned, and the accumulated knowledge, as shown by the work of this Society has placed the entire profession under obligation to it. With this record of unparalleled success we may well venture to prophesy and with better hope of success than our critics enjoyed two decades ago.

To predict what shall be the future of therapeutics we must bear in mind the abandonment of the methods of investigation which obtained twenty years ago which was the determination of what lesions produced given symptoms and signs and from their consideration deduce the method and form of treatment. Morbid anatomy was then largely the basis of therapeutic endeavor. To-day we strive to ascertain what disturbances of function produce symptoms and to determine during life how the body functions; in other words, anatomical considerations have largely been replaced by biological conceptions and for their study laboratory methods have become of increasing importance, and in so far as they explain the mechanism of variations from the normal they furnish the premises upon which we may base conclusions which may be helpful diagnosis and prognosis, and especially as affording valuable indications for therapeutics in the broadest sense.

We require as thorough, accurate, and conclusive laboratory investigations of the effects of climate, the various phnomena of the atmosphere as regards temperature, moisture, and other qualities as they affect human life, of physical agencies, as electricity in its various forms of application, of the Roentgen and other rays, including radium emanations, of the effects of exercise and of diet, of massage, including the more limited in form but violent in quality now in some vogue, of the functions of the endocrine bodies, and of psychological operations as influencing somatic processes now chiefly employed by individuals of abnormal mentality —as those investigations which have been carried out for decades in the domain of pharmacology.

Fundamental to the productiveness of these investigations must be a great improvement in the equipment of the workers and a standardization of the technique especially in the field of biochemistry. For instance, the same specimen of blood should not be reported as Wassermann negative by one, one plus by a second, and three plus by a third observer. The same variations as to blood sugar, purin bodies, or creatinin are by no means unusual. Patience, thorough technical training, and judicial temperament combined, in the laboratory will make for

more confidence in their findings. The conclusions to be drawn must not be entirely left to the laboratory worker, for some are known to possess, and sometimes exhibit, a very vivid scientific imagination. The final conclusion must be arrived at by one who not only knows the methods but as well their limitations, and by correlating these findings with those based upon observations in broader methods of investigation and chastened by practical experience, a more sound decision can be reached and one of greater value in determination of therapeutic measures.

Even in pharmacology the field of usefulness of laboratory investigation may be greatly enlarged. In endocrinology much may be placed upon a firmer foundation. For substances derived from the indigenous vegetable kingdom of extensive use by a well known and earnest group of practitioners, many of important action should be the subject of intensive study, in order that their employment may be more intelligent than is possible from purely empirical tradition. It is needless to remark that the great complexities of chemical composition peculiar to all substances of vegetable origin add to the difficulties in reaching accurate conclusions. Questionnaires have shown that cactus is in frequent use in the treatment of cardiac and circulatory disorders comparing favorably in extent even with digitalis. Yet scepticism as to its value is frequently expressed, based upon the results of laboratory work by an English observer. As his results were so out of harmony with the practice of excellent clinicians, the most important botanist in this country reported that the material used was an interesting plant in no way related to the substance supposed to have been used. Later a laboratory worker in this country undertook another investigation and reported the substance inert. As the conditions under which this investigation was undertaken were peculiar, it would be charitable to suppose that the material employed was not an active one, due to faulty collection and selection or pharmaceutical preparation. Yet any one who knows how to employ instruments of precision can demonstrate that any of the active preparations of this plant possess the peculiar properties of increasing the frequency and force of the cardiac contractures. Such laboratory investigations as these only reflect upon the accuracy, honesty, and general credit of the pharmacologist, and detract from his reliability.

The investigator, assuming that he is competent, thorough, and honest, is useful, even indispensable, in blazing new paths in the domain of knowledge which may be made of practical use. He is equally important in that he may place the methods and material, which have been employed empirically for decades, upon a sure and broad basis.

But the results of laboratory investigation must not be accepted without question; their value must be established by the conclusions based upon actual employment in the practical work in the art of medicine; the clinician pronounces the verdict and upon this the scientific value of laboratory conclusions must stand or fall. From clinical observation we look to the laboratory for explanation, modification of judgment or rejection upon experimental data, but we come back to clinical observation, and this is the basis of therapeutic advance.

In fine the future of therapeutics in its broader sense rests primarily upon the diminishing importance of morbid anatomy with the increasing study of pathological physiology, for pathology is merely physiology which has become abnormal; upon the deductions from intensive work in biological chemistry of more accurate technique, and upon a more searching analysis of clinical results; and upon the intelligent practice of the science of therapeutics may be based the art of therapeutics, which is the aim of all practitioners sincerely devoted to the alleviation of suffering and the cure of disease.

The wonderful advances of the last two decades of the life of this Society in the treatment of infectious diseases, disorders of metabolism, and degeneration in various physical systems, the production of immunity either special or general, and the clarifying of scientific knowledge are an earnest of the therapeutics of the future the basis of which must be established in the carrying out of the essential methods herein set forth. From our past record we can assuredly predict that in the placing of therapeutics, in its broadest sense, upon competent instruction of the student, upon accurate investigation in laboratory, and upon logical analysis of the results of clinical experience this Society will continue to be productive in the dissemination of knowledge of the science and contribute very largely to the practice of the art of therapeutics.

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## DISCUSSION

Dr. Oliver T. Osborne of New Haven expressed his hearty indorsement of the papers by Drs. Reilly and Pottenger and hoped that what had been said would sink into the minds of all.

Dr. James M. Anders of Philadelphia said he was in entire agreement with the positions taken by Dr. Reilly and Dr. Pottenger. As Dr. Reilly had said, we had been swinging away from solely didactic instruction toward clinical teaching until the former was too much neglected, and the reason we should turn the pendulum in the reverse direction, for some distance at least, was that there were so many opportunities at the present day for the student to get practical training after leaving school. He himself wished to emphasize the fact that too much stress was being laid upon the specialties in the undergraduate years of

study. We had standardized undergraduate teaching and had begun to standarize graduate teaching, and one could foresee the time when much of the training now given to the undergraduate would be transferred to the graduate curriculum. Indeed, this tendency had already been established, and it was to be hoped that it would be carried further along, so that the past tendency toward over-specialization would be corrected. Dr. Pottenger had stated the situation correctly when he said that too much consideration was given to the disease and too little to the patient himself. In the speaker's own work as a consultant he rarely found physicians suggesting for overwrought nervous systems and mental worry repose, calmness, and optimism, things that invigorate rather than depress vital function, that increase rather than decrease resistance to disease. Medical schools had not been training the student to recognize the potent influence of the mind upon the body, and for the reasons stated by Dr. Pottenger little or no attention had been given in the past to the socalled applied psychology which would enable the student, when he went into practice, to meet successfully the almost universally pessimistic attitude of patients. There was no doubt that at the present day we were burdened with too many specialties, yet he was impelled to suggest another—namely, "pessimism," with the view of bringing about the cultivation of a cheerful optimism. It was because of a defective education that physicans too often failed to instil optimism into their patients, which was often the best tonic that could be prescribed. He had been glad to hear it urged that physiology should not only be taught to the undergraduates but also by the physician to his patients. For a number of years he had been trying to instruct his own patients in personal hygiene, and he was quite willing to add physiology. Physicians should teach not only their patients but the community in which they live all the hygiene and all the physiology possible as one of the best remedies for all the drugless cults to which the public was rushing like mad. The point which he wished to emphasize was that in the undergraduate school the student should be taught to establish and maintain a system of instruction in personal hygiene and physiology to his patients and the public. In his opinion, the society had a very distinct function to perform with regard to the education and training of men in therapeutics; it was time the members should carefully study their job and recognize that it carried with it great opportunities and grave responsibilities. The society should serve as a guide to the profession in all matters pertaining to therapeutics and so counteract the influence of the various drugless cults and pathies—each with a little virtue behind it—now so numerous and so popular that they actually cared for one-third of the population of the United States. The state should be made to recognize the fact that certain fundamental branches, *e. g.* anatomy, physiology, chemistry, and pathology, were necessary, no matter what practical system of the healing art the individual student wished to pursue in the future. It should be quite possible to combine the institutional interests, so far as the instruction of medical students in these basic scientific branches is concerned, and thus in one sweep speedily do away with the various cults. This society should be able to bring about the teaching of therapeutics and of the management of disease in general in our medical schools in a maner so broad and full as to leave little room for the pathies and drugless cults.

Dr. Louis F. Bishop of New York said that a great change had taken place in the profession. In the old school all were taught that disease consisted of pathological anatomy and certain anatomical lesions. That school had more or less

passed away and was being repaced by pathologic physiology—that the changes in pathological anatomy were the end result of disturbances in the physiology. That was very hopeful. In his own particular subject of the heart this tendency was very strong. Nothing had done more to abolish therapeutic nihilism than the technical observance of the disturbed heart and the possibility of recording the disorder as it appeared, and then applying the proper treatment. Probably the study of fibrillation had done more to destroy therapeutic nihilism than anything else in the last fifty years, for that so definitely showed the effect of a drug on a disordered condition. With regard to the psychological management of patients, he had adopted the plan of absolute frankness with every patient he came in contact with. Hardly a day passed that some doctor or relative of a patient did not say to him. "If you find anything definite, please don't tell the patient." He would reply that if they wanted anything concealed they must take the patient to someone else. He had found that by a policy of complete frankness he could get the cooperation of the patient. He would always say: "I hope and believe that you will improve under treatment." If one asked: "Am I liable to sudden death?" he would reply: "Yes." It was a curious fact that many hundreds of persons had accepted the fact, discounted it, and had forgotten it—had stopped worrying about it. It was very like life insurance; everyone knew he was subject to death, but he did not believe that it was going to happen to him, and so would not insure. By absolute frankness one could get the cooperation of the patient. If he was told you knew he was in danger, but hoped and believed he would get better, the fear would be discounted. In regard to educating people in regard to physiology and disease, Dr. Bishop said that for thirty-five years he had been active in the Society for Instruction in First Aid to the Injured, but every time he had tried to write some public article he had gotten it in the neck from the profession for trying to advertise his own practice. That was not fair. It was the duty of the profession as far as possible to instruct the public in such matters, and there ought to be some way in which such work could be censored before it got to the public so that reproach could be avoided. The *Journal of the A. M. A.*, in criticising his last book, said that it was very fine work, but it meant that Dr. Bishop wanted the people to go to him. The American Medical Associaton was perfectly willing that anyone whom it might designate should take part in public health education, but if anyone else did it, it was self-advertising. It was difficult to examine into a man's motives, but that was no reason why every effort should not be made to disseminate true medical information as far as possible. Everyone in the community should be taught first aid to the injured and the first principles of pathological physiology and prevention of disease.

Dr. Charles E. de M. Sajous said that in expressing his admiration for the papers presented by Drs. Reilly and Pottenger he wished to recall that therapeutics was being neglected to a material degree in our medical schools because it was still empirical and unscientific, even though pharmacologists contributed much to our knowledge. In his presidential address last year he had urged the fact, now conclusively established, that many drugs, the iodides and strychnine, for instance, produced their beneficial effects by stimulating certain ductless glands, and that it was through these glands that the curative power of several of our best remedies was exercised. This therapeutic method (see Medical Record, Sept. 18, 1920), which Doctor Sajous had termed "pharmacoendocrine therapy," was of capital importance to the practitioner—sufficiently so, in fact to have caused the

London *Lancet* to recommend the study of endocrinology in this connection by the new chair of pharmacology to be founded at St. Mary's Hospital Medical School of London. The University of Pennsylvania had, however, taken the lead in this respect, its Graduate Medical School, at the request of our fellow member, Prof. James M. Anders, and its Medical Faculty, having created a chair of Applied Endocrinology, the first, by the way, in the history of medicine, to which the speaker deemed it a great honor to have been appointed.

Dr. Spencer L. Dawes of New York said that for many years he, like Dr. Osborne, had been "a voice crying in the wilderness" in regard to teaching therapeutics and physiology. It seemed to him that the main point had been lost sight of. The fact was it was not taught, and he defied anyone to point out more than one of ten schools that was teaching any therapeutics. They did not teach it. As he had himself said in a paper read at Atlantic City, they taught two things—to make a diagnosis and to make an autopsy to prove the diagnosis, and if they could teach only one thing, they taught them to make the autopsy. They did not care whether they cured disease or relieved the patient. It was well to know pathology and diagnosis, and how to look through a microscope, but the physician ought to know how to help the patient. Until he went back to first principles and taught therapeutics we would not accomplish what we were after. If one went to the medical schools today and asked the student what he was interested in, he would not find one in a thousand interested in the cure of disease, but only in surgery, otology, laryngology, etc. Dr. Dawes said he had taught in the medical schools for twenty years, and there was not one that taught therapeutics as it should be taught. Until we got back to teaching therapeutics, nothing would be accomplished. Another point was valuable. You might have your full-time man, but when you put in your whole lot of full-time men in the medical schools you would be losing sight of the man's personality, of the man who approached disease at the bedside and told the student how to treat disease—not as in the hospital, where directions were written and the nurse was told how to treat disease. The nurse would see that it was done. But how about the physician when he visited a private patient and told him to take something, and the patient would say: "I don't want to take that"; what would he do then? He would substitute something else. The student would not get that knowledge in the hospital, and would not get it until he was taught how to treat disease.

Dr. Jacob Diner said that no more proper subject could be brought before the society than the matter of therapeutics and the teaching thereof. Dr. Dawes found fault that there was no therapeutics taught in the schools. Dr. Diner said he would agree to that and more than that, that whatever therapeutics was taguht was taught on a false basis. The main object seemed to be to cover the text-book, with every drug mentioned. He had seen valuable time wasted by teachers on some drug that experienced men had never heard of, simply because the literature somewhere mentioned that drug. One thing was rarely taken into consideration, the drug known as common sense and its application to the treatment of disease. That was a question often lost sight of. Another error often found in the teaching of the subject was absolutism of teaching and giving the student formulas which were "sure cures" for this, that, and the other thing. That reminded him of a story of a very good and careful observer who took detailed bedside notes of his patients. He had a case which presented a certain symptomcomplex, and from

day to day he watched the case and put down the remedial agents employed and what else he did for the patient. The patient did not get better; and finally one day, when calling, the patient's wife said to the doctor: "What do you think August asked for today? He wants pig's knuckles, sauerkraut, and beer." And the doctor said: "Let's make his last days happy and give it to him." The next day he called on the patient, expecting to find a crape on the door, but August was sitting up, smoking, reading the paper, and enjoying life as much as ever; and the doctor put down in his notebook beneath the carefully recorded bedside notes: "Pig's kunckles, sauerkraut, and beer, sure cure." A short time after, Pat was taken sick, and the doctor prescribed pig's knuckles, sauerkraut, and beer, telling Bridget that this was bound to cure Pat. But the next morning Pat was dead—and the doctor added to his previous notes, after the words sure cure, "for the Germans, but it's hell on the Irish."

Dr. William Fitch Cheney of San Francisco expressed his agreement with what Dr. Reilly had said in regard to the swinging of the pendulum toward more therapeutic instruction. He had been through that experience himself. The teaching of former years was almost entirely didactic; now it was almost entirely clinical, but the students of today were not so thoroughly conversant with the cure of patients and disease as those of former days. He believed in compromise; they should have both. He was also in agreement with what Dr. Pottenger had said. It did not matter how much the physician knew of diagnosis, pathology, materia medica, the doses and qualities of drugs, his success as a practitioner came down to a question of personality; the man who knew it all might be a dismal failure, and the other a great success. The man with underlying optimism, who was ready to give his patients encouragement, would attain a success which the man who treated his patients overmuch with drugs would never reach. There were two classes of patients—those who had no serious illness and who would get well, and those who could not be cured. We could do an immense amount of good to patients who were not seriously ill; they were inclined to think they were very much worse than they really were; as Mark Twain said, one-fifth is real and the other four-fifths what he thinks. If you were convinced that the patient was not seriously ill, you could take away that four-fifths by reassurance and sympathy and common sense. Those in the other group, who had serious illness that could not be cured with drugs—but might be made worse—could also be helped by common sense and telling them the truth. Death was not the worst that could happen to a man; it was often a relief to one who was suffering, but he could be greatly helped by the exercise of common sense and reassurance, making him feel that the very best possible was being done to make him comfortable and prolong life. Dr. Cheney said he knew from observation that the brilliant student was not always the best prepared for practice, but that was one reason why men who were not well prepared were able to do for the patient what the well-prepared scientific man did not always do.

Dr. William F. Milroy of Omaha expressed his commendation of the two papers. He had heard this theme developed to the same extent in an experience meeting. He had taught for thirty-five years, and was delighted to hear this discussion; for quite a long time he had felt almost afraid to suggest anything along this line in the society meetings. One was apt to be counted an old fogey, a "has-been" if he harked back to the methods he had found successful; but it was the duty of the society to promulgate authoritatively the views expressed in these

papers and the discussion. He had been convinced that medical education was a lamentable failure in a large degree, owing to this devotion to the specialties and to the excessive stressing of laboratory work at the expense of the practical we had been taught and had found successful.

Dr. Reilly said that he and Dr. Pottenger felt that they had been sitting for the time being in the criminal dock, but, because of the general approbation expressed by so many teachers of medicine, they were very glad, indeed, that they had been discharged as not guilty.

Dr. Pottenger said he wished to emphasize the importance of maintaining the psychical as well as the physical side of the patient. It was noted in practice, but not in teaching. Nothing would do more for a chronic invalid than hope. He then cited the case of a doctor who developed tuberculosis and consulted two or three of the best physicians in a large eastern city, who made a diagnosis and told him to go west, which he did; but gave him no hope for recovery. One year later he came to Dr. Pottenger, who examined him and at once told him that he could be restored to health. This doctor then said to him: "That is the first word of hope I have heard for a year." He said that he was giving up his profession, for he would not belong to a profession that could give no hope. The man who neglected that factor was neglecting one of the biggest factors in cure. He himself would rather treat a patient with hope in a closed room than with discouragement in the open air.

## CONSTITUTION AND BY-LAWS.

### ARTICLE I.

This Society shall be known as the American Therapeutic Society.

### ARTICLE II.

The object of this Society shall be the promotion of therapeutics in its broadest sense.

### ARTICLE III.

This Society shall meet annually at such time and place as the Council may determine.

### ARTICLE IV.

Section 1. The Officers of this Society shall consist of a President, three Vice-Presidents, a Secretary, a Treasurer, and a Council of fifteen members, all to be elected from the active membership, by ballot, at an annual meeting.

Section 2. The Council may be convened at any time by the Chairman, at the request of any three of its members. Its decisions shall be equivalent to acts of the Society, and shall be reported to it at the next regular meeting. The Council shall elect from its members a Committee on Admissions to consist of three members.

Section 3. A vacancy occurring in any office may be filled by the Council.

### ARTICLE V.

Section 1. (a) This Society shall consist of not more than one hundred active members.

Section 1. (b) There shall be established an Associate Membership, proposed and elected in the usual manner, paying the same dues as Active Members and having all the rights and privileges of Active Membership, except that Associate Members shall not hold office or vote. Such Associate Members shall become Active Members, on recommendation of the Council and by vote of the Society, as vacancies occur in the list of Active Members and in the order of their Election.

Section 1. (c) There shall be created a class of members to be known as "Fellows." On recommendation of the Council and with the approval of the Society, any member in good standing who has belonged to the Society for not less than ten years and who by reason of age or other well founded causes, is prevented from actually participating in the work or meetings of the Society,

may be created a Fellow. Such Fellows, shall be entitled to all the rights and privileges of membership except that of holding office and voting and shall not be called on to pay dues.

SECTION 1. (d) Honorary members may be elected on recommendation of the Council.

SECTION 2. Any qualified physician engaged in the general or special practice of medicine or surgery, or in laboratory research of interest in the treatment of disease is eligible for membership.

SECTION 3. Applications for membership should be made in writing at least one month before the annual meeting. They are to be referred to the Committee on Admissions, which shall, on approval, present their names to the Society at the annual meeting. Five negative ballots shall reject an applicant.

SECTION 4. Applications for membership shall be accompanied by the annual dues for the ensuing year.

SECTION 5. Resignation of members shall not be accepted until all dues have been paid.

## ARTICLE VI.

All proposed changes of the Constitution must be offered in writing at a regular meeting. They are to be considered only at an annual meeting, when a two-thirds vote of the members present shall be necessary for their adoption.

## By-Laws.

1.

The *President* shall preside at the annual meeting of the Society, and deliver an address. He shall appoint a Committee on Scientific Business and a Committee of Arrangements.

In the absence of the President, one of the Vice-Presidents shall preside.

2.

The *Secretary* shall keep a record of the transactions of the Society and of its Committees, conduct all correspondence of the Society, and mail to each member a programme of the meeting, at least two weeks before it is held. The records, publications and seal of the Society shall be in his custody.

The *Treasurer* shall collect all moneys due the Society, disburse the same, as directed by the Council, keep a proper account of all his transactions, and render an annual statement to the Society. He shall have charge of all property belonging to the Society not otherwise provided for.

3.

Ten active members shall constitute a quorum for the transaction of business.

4.

SECTION 1. The *Council* shall constitute a standing committee to consdier all matters of interest to the Society. It shall elect a Chairman, Vice-Chairman and a Secretary, and shall appoint an Editor of the Transactions.

SECTION 2. Three members of the *Council* shall be elected annually by the Society, each to serve five years.

SECTION 3. Five members shall constitute a quorum.

5.

The *Committee on Admissions* shall investigate the qualifications of applicants and report at the next annual meeting.

6.

Charges against any member must be made in writing. They shall be referred to the *Council* for investigation.

7.

No papers, report, abstract or other communication, either written or verbal, which, directly or indirectly, commends or advocates any secret, patented or trade-marked product or method of treatment shall be presented to or received by the Society; nor shall any discussion on such product or method be permitted.

Papers are limited to twenty minutes and discussions to five minutes.

8.

The *annual dues* shall be ten dollars, payable in advance.

9.

The *order of business meetings* shall be as follows:

1. Reading of Minutes.
2. Reports of Officers and Committees.
3. Election of Members.
4. Presentation of Communications.
5. Miscellaneous Business.
6. Election of Officers.

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